Non-surgical options to treat androgenic alopecia

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Abstract

Androgenic alopecia (AGA) is the commonest cause of hair loss in men and women. It is attributed to genetic and hormonal factors. This paper aims to discuss three non-surgical options to assess their use and effectiveness in treating AGA. This will include the following treatments: Minoxidil, Finasteride and low-level laser therapy (LLLT).

Key words: Androgenic alopecia, Minoxidil, Finasteride, low-level laser therapy (LLLT

Introduction

Androgenic alopecia (AGA) is the commonest cause of hair loss in men and women [1]. It is attributed to genetic and hormonal factors. A major factor identified, so far, is the effect of Dihydrotestosterone (DHT) on the scalp hair follicles. DHT is formed by the conversion of Testosterone to DHT when it is activated by the enzyme 5-α reductase which is found in type 2 receptors on the scalp hair follicles. The result of this activation is miniaturization (thinning) and shortening of the growth phase (anagen) in the hair cycle [1].

This paper aims to discuss three non-surgical options to assess their use and effectiveness in treating AGA. This will include the following treatments: Minoxidil, Finasteride and low-level laser therapy (LLLT).

Formulation of the three-part BET question:
[Non-surgical treatment] is [Effective and safe] at [treating androgenic alopecia]

- Patient group: Patients with androgenic alopecia
- Defined question: can non-surgical, minoxidil, finasteride and LLLT treat androgenic alopecia
- Relevant outcome: improve androgenic alopecia (AGA)

Clinical scenario: A patient with androgenic alopecia presented to the clinic. He/she wanted to discuss the available non-surgical options to treat his/her AGA as he/she has needles phobia and is not keen on surgery or injections.

Search strategy:
Medline search using PubMed (restricted to publications from 2005-2020). Also, a manual search in Google scholar was conducted.

Search outcome:
Initial PubMed search resulted in 26 publications; among these, three papers were found to be relevant to this topic. Three more papers were manually searched in Google scholar (Olsen et al., Kaufman et al. and Lee et al).

Relevant papers: Low-level laser table

Author, date & country	Patient Group	Study type (level of evidence)	Outcomes	Key Results	Study weaknesses
A.K Gupta et al. Efficacy of non-surgical treatments for androgenetic alopecia: a systematic review and network meta-analysis 2018 Canada	15,888 participants (88% males), average age 36.0 ± 7.3	1a Systematic review	LLLT is superior to placebo in treating AGA	5 RTCs showed that LLLT has the highest effect in increasing average hair count compared to placebo among all non-surgical options. (the difference in hair count = 66.70)	All 5 trials were funded by the device manufacturer or they had an affiliation to the authors.
Evan Darwin et al. Low-level laser therapy for the treatment of androgenic alopecia: a review 2017 USA	13 RCTs	1a systematic review	LLLT is safe and effective in treating AGA. LLLT can be used alone or in combination with finasteride 1mg or topical minoxidil 5%. Overall LLLT is safe, however, in 5 trials AEs were reported i.e., urticaria, skin dryness, acne, headache and mild burning sensation.	10 RCTs showed a significant statistical increase in hair count (20 hair/cm2), this is higher than the growth rate seen in both finasteride 1mg and Minoxidil 5% (13.5 and 12.3 hair/cm2 alternatively)	Early RCTs were small and lacked control, more recent RCTs were better designed.

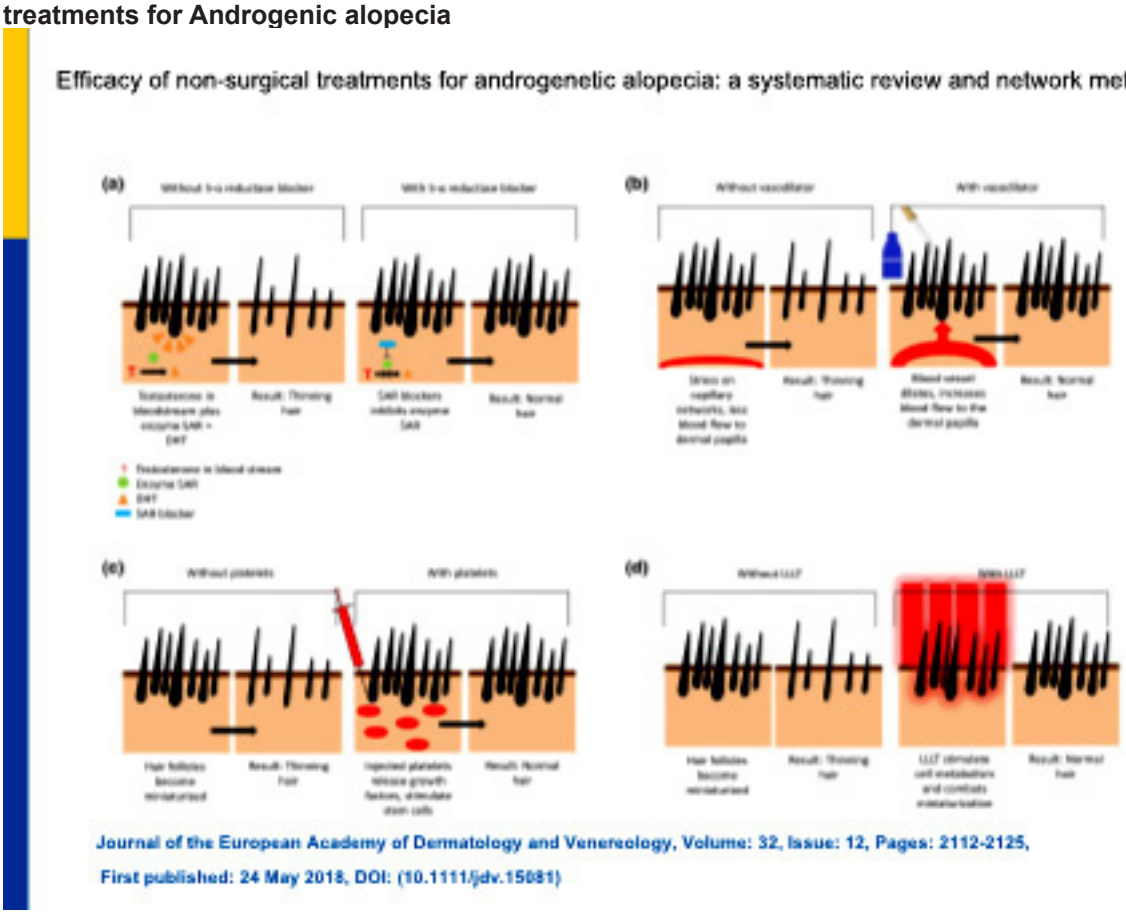
Relevant papers: Minoxidil table

Author, date & country	Patient Group	Study type (level of evidence)	Outcomes	Key Results	Study weaknesses
A.K Gupta et al. Efficacy of non-surgical treatments for androgenetic alopecia: a systematic review and network meta-analysis 2018 Canada	15,888 participants (88% males), average age 36.0 ± 7.3	1a Systematic review	Topical Minoxidil5% and 2% were both superior to placebo in treating AGA	Minoxidil5% showed a higher average hair count when compared to Minoxidil2% (4.69 [1.35, 8.04]), however, it carries the greatest risk of adverse events (n=45)	
Olsen et al. A multicentre, randomized, placebo-controlled, double-blind clinical trial of a novel formulation of 5% minoxidil topical foam versus placebo in the treatment of androgenetic alopecia in men 2007 USA	352 men, age (average age 39 years old), 86% Caucasians(172 on placebo arm and 180 on 5% Minoxidil foam)	1c RCT	At 16 weeks there was a statistically significant rise in hair count with minoxidil 5% foam compared to placebo (hair count 20.9 vs 4.7 respectively) (p<0.001	Subjectively participants reported a 70.6% improvement in hair growth compared to 42.4% in the placebo arm. Overall, there were less Adverse Events AEs seen in comparison to minoxidil solution (less than 1%) including irritation, headache, acne	Short duration for the study, only involved male patients and there was no data collection beyond 16 weeks. Some authors received funding or were employed by Pfizer.
Zhou et al. The effectiveness of combination therapies for androgenetic alopecia: A systematic review and meta-analysis 2020 China	1172 participants	1a Meta-analysis and systematic review of 15 RCTs	The combined therapy of topical minoxidil 5% with finasteride or LLLT is more effective than monotherapy. There was not an increase in adverse effects compared to monotherapy.	Statistically significant increase in hair count with combined treatment for AGA compared to monotherapy. (p <0.05)	

Relevant papers: Finasteride table

Author, date & country	Patient Group	Study type (level of evidence)	Outcomes	Key Results	Study weaknesses
A.K Gupta et al. Efficacy of non-surgical treatments for androgenetic alopecia: a systematic review and network meta-analysis 2018 Canada	15,888 participants (88% males), average age 36.0 ± 7.3	1a Systematic review	Finasteride 1mg (male) is superior to placebo in treating AGA	5 RCTs showed an increase in average hair count of 17.37 compared to the placebo	
Kaufman et al. Long-term treatment with finasteride 1 mg decreases the likelihood of developing further visible hair loss in men with androgenetic alopecia (male pattern hair loss) 2008 USA	1553 participants	1a systematic review of 2 phase 3 trials of men with AGA who received finasteride 1mg vs placebo for up to 5 years.	There is significant statistical evidence that supports the continued use of finasteride 1mg to maintain improvement in hair count and coverage ($p<0.001$)	93% of patients who received finasteride 1mg for 5 years reported no further hair loss compared to placebo ($p<0.001$)	Only included male patients.
Lee et al. Adverse Sexual Effects of Treatment with Finasteride or Dutasteride for Male Androgenetic Alopecia: A Systematic Review and Meta-analysis. 2019	4,495 male participants	1a systematic review of 15 RCTs	In general, 5α-reductase inhibitors increase the risk of sexual dysfunction by 1.57-fold (95% CI) 1.19–2.08).	Finasteride carries a higher relative risk of sexual dysfunction when compared to Dutasteride (1.66 and 1.37 respectively)	Regarding Dutasteride, only 5 papers were meta-analysed as it a newer intervention, hence not many adverse effects were recorded compared to finasteride

Figure 1: summarises the current hypotheses regarding the mechanism of action of different non-surgical treatments for Androgenic alopecia



Comments

This paper looked into the three FDA approved AGA treatments so far;

1. Low-level laser therapy LLLT: These devices emit red light (650–900 nm and 5 mW), which stimulates keratinocytes and fibroblasts mitosis, increases cellular metabolism, reduces nitric oxide level and inhibits inflammation in the scalp [1].

In terms of its efficacy, LLLT was approved by FDA in 2011 and it is ranked as the most effective treatment out of all non-surgical options. Clinically LLLT results in improving hair thickness and hair count by 20 hair/cm2. There were no adverse events reported by patients [1].

Different devices are FDA approved and available commercially i.e HairMax Lasercomb®, TOPHAT 655®, and the Capillus® laser caps. These devices can either be used in clinics or patients can buy them individually. Duration for use depends on the device but roughly patients have to use it for < than 30 minutes up to 3 times a week and can be used in combination of both minoxidil 5% and finasteride for an even better result [3].

2. Minoxidil: Topical minoxidil has been used in improving AGA since the 1980s and it was the first AGA treatment to get FDA approval in 1988. Although the exact mechanism is not known, it is believed that topical minoxidil promotes hair growth by improving blood supply to the hair follicles, by shortening the telogen phase and prolonging the anagen phase in the hair growth cycle [1].

In terms of efficacy minoxidil, 5% has a similar profile to Finasteride 1mg and is more effective than Minoxidil 2%. Regarding, adverse events, minoxidil 5% carries the highest risk of SE among the three FDA approved options (n=45), these AEs include dryness, irritation, acne and headache [1].

It can be used by both genders daily for up to 6 months before expecting enough improvement. Improvement reported in patients with Norwood grade 5 AGA. Commercially it is available in solution or foam forms (foam is a newer version and reported to cause fewer side effects and improved compliance in patients as it gets absorbed more quickly through the skin) [3].

The combined therapy of topical minoxidil 5% with finasteride or LLLT is safe and more effective in treating AGA than monotherapy [4].

3. 5 alfa reductase inhibitors (5-ARIs): Oral Finasteride 1 mg (Propecia) was approved by the FDA in 1997. Currently, both Finasteride 1mg and Dutasteride 0.5mg tablets (unlicensed) for up to 48 to 52 weeks are used to treat male pattern AGA. These oral medications prevent the conversion of testosterone to its active form Dihydrotestosterone (DHT), which lead to a significant drop in the scalp and serum DHT levels by 60-70% [1].

A large meta-analysis (Gupta et al.) showed a statistically significant increase in hair count in men who were treated by both Finasteride 1mg and Dutasteride compared to placebo, giving a clear indication of their efficacy in treating AGA.

Finasteride can be used safely in combination with LLLT or Minoxidil which enhances its effect and produces an even better result than monotherapy [4].

Due to its potential adverse effects on the foetus as well as endometrial and menstrual side effects, Finasteride was not licenced by the FDA for female pattern AGA. Adverse effects in men were less common than with Minoxidil but they were more significant and has a greater impact on patients. These included sexual dysfunction including erectile dysfunction, reduced libido and ejaculatory dysfunction [1].

Current data from Lee et al. estimates the overall risk of 5-ARIs in causing sexual dysfunction at 1.57 folds. Finasteride carries a slightly higher risk than Dutasteride (1.66 vs 1.37 respectively). Data regarding Dutasteride are less consistent due to the lack of enough studies into its use in AGA so far. This might change with more research and studies [5].

Clinical bottom line and Conclusion

LLLT, finasteride 1mg and Minoxidil 5% are all FDA approved for the treatment of AGA. LLLT has produced the best results when used to treat AGA so far and had no reported adverse effects. Minoxidil 5% and Finasteride have similar efficacy but varies in terms of adverse effects. Minoxidil associate with a higher risk of adverse effects which are mainly dermatological, while Finasteride's main adverse effects were sexual dysfunction which can be very frightening to young men who are suffering from AGA. Thorough counselling, good patient selection and tailored treatment are paramount when offering hair loss treatment. Combined treatment is safe and offers a better result than monotherapy.

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