The efficacy of 1550-nm fractional Erbium-glass laser in androgenic alopecia: A systematic review and meta-analysis

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Abstract

This systematic review and meta-analysis aimed to evaluate the efficacy of 1550-nm Erbium glass fractional laser in treating androgenetic alopecia in both men and women for improving hair density and hair shaft diameter. A systematic review was conducted. PubMed, Embase, and Cochrane were searched up to December 2019, with no lower limit on the year. We included prospective trial, semi-experimental, randomi ze control trial, interventional study on human study. Four articles including 278 participants which treated with 1550-nm Erbium glass laser were selected for our analysis, all studies evaluated the change in hair density and hair shaft diameter. It's found a statistically significant hair density and hair shaft diameter increased in the 1550-nm Erbium glass laser group. The overall SMD regarding changes in hair density was 25.26 (95% confidence interval CI 8.62 to 41.89) the P=0.003 and the SMD heterogeneity the I^2 was 98%. Whereas, the change in hair shaft diameter, the overall SMD was 2.03 (95% confidence interval CI 0.91 to 22,14) the P =0.0004 with the SMD heterogeneity I^2 was 92%, suggested that this treatment provided an essential result in increasing hair shaft diameter and hair density without any harmful effect.

Keywords: *Androgenic alopecia, Systematic review and meta-analysis, 1550-nm Erbium glass fractional laser, fractional laser*

1. Introduction

Androgenic alopecia is the most common type of progressive hair loss. This is a common condition in which the decreased hair amount fails to cover the scalp adequately and can cause psychosocial distress (Cash, 1992; Mubki et al, 2014). Incidence and prevalence of AGA depend on age and race. Based on the little prevalence data available, we know that up 30% of white men will have AGA by the age of 30 years, up to 50% by 50 years, and 80% by 70 years (Hamilton, 1951; Severi et al, 2003). Chinese, Japanese, and African American people are less affected than Caucasians (Otberg et al, 2007). Hair follicles (HFs) undergo cyclic degeneration and regeneration throughout life (Chuong et al, 2012): they cycle through anagen (growth), catagen (involution) and telogen (resting) phases and then re-enter anagen. HF stem cells (HFSCs) are located in a unique structure of HF epithelium: the bulge area (Hsu et al, 2104; Cotsarelis et al, 1990). The hair growth is highly coupled with the activity of HFSC: HFSCs are activated in late telogen to early anagen and the activation of HFSCs fuel the growth of hair follicles (Greco et al, 2009; Rompolas et al, 2012). Androgenic alopecia is generally divided into two categories: scarring alopecia and nonscarring alopecia (Sellheyer & Bergfeld, 2006). AGA is characterized by the androgen-mediated miniaturization of terminal hairs to vellus hairs (Garza et al, 2011). Notably, the exact mechanism of how the 1,550-nm Er: Glass fractional laser induces new hair growth is still unknown. Fractional photothermolysis were developed from selective photothermolysis, which is the basic mechanism behind most laser and lightbased devices (Narurkar, 2009).

The non-ablative fractional 1550-nm Erbium-glass laser has been evaluated for the treatment of androgenic alopecia in women and men because it can penetrate the scalp more effectively than other lasers and does not induce bleeding. Like other fractional lasers, its method of action involves producing

microcoagulative wounds in the dermis. Penetration depth and wound size while using this laser can be controlled with a fractional near-infrared laser. The wound healing process associated with this treatment believed to be due to the stimulation of hair regrowth. Both the Wingless-related integration site (Wnt) proteins and insulin-like growth factor 1 (IGF-1) are important molecules that promote new hair growth (Meephansan et al, 2018).

Currently, the new treatment have been launched for AGA, including the 1,550-nm Erbium-glass (Er:Glass) fractional laser (lee et al, 2011, Cho et al, 2013). In 2011, Lee and colleagues (lee et al, 2011) demonstrated significant increases in hair density and hair thickness using this treatment, the study revealed the improvement in hair growth and reported the upregulation of Wnt10A at 24 hours after irradiation with fractional laser in patients with AGA (Kim et al, 2011) Notably, the mechanism of how the 1,550-nm Er:Glass fractional laser induces new hair growth is still unknown. Interestingly, there were some reviews about the efficacies of treatment modalities in AGA. However, the outcomes of comparing different types of treatment in AGA have not properly summarized yet. Additional studies evaluating the stability and effects of this laser therapy should be conducted to confirm its mechanism of action and effectiveness (Kim et al, 2011)

2. Objectives

This systematic review aimed to evaluate the efficacy of 1550-nm Erbium glass fractional laser in the treatment of androgenetic alopecia for improving hair density and hair shaft diameter in both men and women who were diagnosed as AGA.

3. Materials and Methods

Systematic review

This systemic review and metanalysis were conducted in agreement with the 2015 modified 32 item PRISMA extension statement for network meta-analysis (NMA) (Hutton B et al, 2015). The PubMed and Google Scholar databases were searched using the terms "androgenetic alopecia" and "fractional laser" on 7 October 2019. Four studies which investigated the use of 1550-nm Erbium glass fractional laser as treatment for AGA were identified. The studies that was included must be followed by the inclusion criteria such as androgenic alopecia with all age group and both sexes. The studies designed were clinical trial, cohort studies, case control studies and Human study which were written in English as well as the full text articles. The remaining human studies will be described in the form of a meta-analysis where possible. Only four studies that met the inclusion criteria and considered for inclusion in the meta-analysis. Additionally, measures of treatment success were diverse, many of which used subjective evaluation. The resulted in four studies with adequate data to be included in the meta-analysis (pooled N=278 participants). In these studies, hair density and hair shaft diameter were the measure of treatment success. The meta-analysis examined the standardized mean difference overall and for each of the four studies using a forest plot, taking into consideration heterogeneity as measured by I2 statistic.

4. Results

The present metanalysis focuses the hair density and hair shaft diameter improvement the efficacy of androgen alopecia (AGA) patients who were treated by 1550nm Erbium glass fractional laser. We concluded 4 studies that recruited AGA patients and receiving 1550nm Erbium glass laser treatment. AGA patients following the treatment has a significant increase in both hair density and hair shaft diameter. The articles were published between 2011 to 2019. In sum, the number of the participants included was rang from n=27 to n=47 in each study and a total of 278 were included. Both male and female patients who was diagnosis with AGA were included in this study.

1550nm Erbium glass fractional laser studies

The pools random effects interval variable (IV) for AGA patients treated with Erbium glass fractional laser, by study design, were showed in Fig.1. The overall of the studies was 25.26 (95% confidence interval CI 8.62 to 41.89). In the other hand, the change in hair shaft diameter, the overall SMD was 2.03 (95% confidence interval CI 0.91 to 22, 14) (fig.2). The result indicated the significant increase in hair density (overall P=0.003, I2=98%) and hair shaft diameter (overall P = 0.0004, I2=92%).

Subgroup analysis

Firstly, A study by Lee in 2011 which recruited only female patients was treated on 27 male who were diagnosed as female pattern hair lose showed a significant in increasing in both hair density and also hair shaft diameter, with hair density from the baseline was 100±14□cm2 and increased to 157±28□cm2 (57.00 of 95% confidence interval CI 45.19, 68.81) and the hair shaft diameter MSD was 58 ± 12µm to 75 ± 13µm (17.00 of 95% confidence interval CI10.33, 23.67) (Lee et al, 2011).

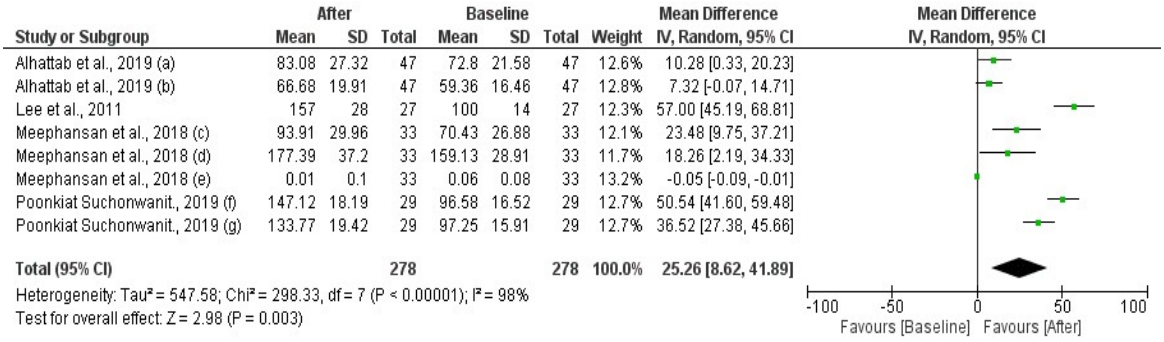
Secondly, by the year of 2018 Meephansan performed a study which was included the outcome of the increase in hair density of terminal hair, non-vellus hair, vallus:non-vellus hair and hair shaft diameter also showed a significant increased after 12 sessions by 2 weeks interval of 1550nm Erbium glass fractional laser treatment in both man and women, the result of density of terminal hair in the baseline was 70.43 ± 26.88/cm2 to 93.91 ± 29.96/cm2 (23.48 of 95% confidence interval CI 9.75, 37.21), non-vellus hair was 159.13 ± 28.91/cm2 to 177.39 ± 37.2/cm2 (18.26 of 95% confidence interval CI 2.19, 34.33), vellus:nonvellus was 0.06 ± 0.08 to 0.01 ± 0.1 (-0.05 of 95% confidence interval CI -0.09, -0.01) and hair shaft diameter was 42.52 ± 9.82 µm and increased to 50.74 ± 10.69µm (8.22 of 95% confidence interval CI 3.27, 13.17) (Meephansan et al, 2018).

Moreover, in 2019, A study of male patients by Suchonwanit, which only included 29 males who had AGA from grade 3 to grade 4 with the 24 weeks of treatments duration and 2 weeks interval in each intervention with monotherapy and combination therapy showed significant increase in both hair shaft diameter and hair density. The hair density of the combination therapy side the baseline was 96.58 ± 16.52hairs/cm2 and increased to 147.12 ± 18.19 hairs/cm2 (50.54 of 95% confidence interval CI 41.60, 45.66), monotherapy the base line was 97.25 ± 15.91 hairs/cm2 increased to 133.77 ± 19.42 hairs/cm2 (36.52 of 95% confidence interval CI 27.38, 45.66), while the hair shaft diameter of combination therapy side was 50.93 ± 13.59µm increased to 67.28 ± 15.63µm (16.35of 95% confidence interval CI 8.81, 22.14) and the monotherapy of hair shaft diameter at the baseline was 51.16 ± 14.53 and increased to 65.32 ± 16.42µm (14.16 of 95% confidence interval CI 6.18, 22.14). The result is indicated that Erbium glass fractional laser can improve hair thickness and hair shaft diameter with no significant different in both men and women (Suchonwanit et al, 2019).

Lastly, in 2019 Alhattab was included as male and female treated with Erbium glass fractional laser shows a significant increase in both male and female group, 26 female show a significant increase in hair density from the baseline of MSD 72.8±21.58 to 83.08±27.32 95% (10.28 of 95%confidence interval CI 0.33 to 20.23) and the hair shar diameter from the baseline of MSD 3.12±0.43 and significant increased to 3.84±0.51 (0.72 of 95% confidence interval CI 0.53, 0.91) after the treatment of 10 sessions, 2 weeks interval. 25 male patients showed a significant increase in hair density from the baseline of MSD 59.36±16.46 and increased to 6.68±19.91 (7.32 of 95% confidence interval CI -0.07, 14.71) and hair shar diameter from the baseline of MSD 2.68±0.56 to 3.29±0.7 (0.61 of 95% confidence interval CI 0.35, 0.87) (Alhattab et al, 2019).

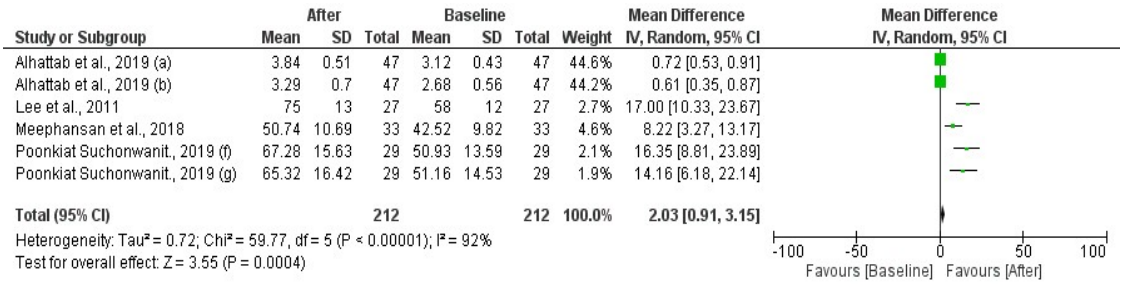
Table 1 Characteristics of studies included in the meta-analysis

First author	Study design	Total no. of subject	Machine name	Protocol/ parameter and frequency	Treatment duration and interval	AGA and another combination therapy	Outcome hair density	Outcome hair shaft diameter
Lee et al, 2011	Prospective trial	227	Musac, Lutronic	5-10mm, 6mj, 800spot/cm^2	20 weeks, 2weeks interval	None	P<0.001	P<0.001
Meephasan et al, 2018	Semiexperimental	223	Musac, Lutronic	2*12mm, 6mj, 300spot/cm^2	24 weeks, 2 weeks interval	None	P=0.001	P=0.27
Suchonwanit et al, 2019	RCT, blind split scalp	229	Finescan, TNC meditron	7mm, 6mj, 300spot/cm^2	24 weeks, 2 weeks interval	1550-nm with minoxidil, minoxidil alone	P=0.004	P=0.34
Alhattab et al, 2019	Interventional study	447	Quanta system SPA	7mm, 6mj, 1HZ frequency	20 weeks, 2 weeks interval	None	P=0.001	P=0.001



Footnotes
(a) Women
(b) Men
(c) Terminal hair
(d) Non-vellus hair
(e) Vellus:non-vellus hair
(f) Combination therapy
(g) Monotherapy

Figure 1 Meta-analysis of hair density by study design. IV, interval variable; random; CI, confidence interval



Footnotes
(a) Women
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(e) Vellus:non-vellus hair
(f) Combination therapy
(g) Monotherapy

Figure 2 Meta-analysis of hair shaft diameter by study design. IV, interval variable; random; CI, confidence interval

5. Publication bias

Figure 3 and 4 showed the filled funnel plot of all the studies regarding the increasing in hair density and hair shaft diameter in this meta-analysis. These funnel plots had shown very positive outcome, but it seems to have a large variation of the positive outcome, it may due to the differentiation of the results in each patient. In fact, the outcome we received in each study revealed that in female and the younger age had shown higher outcome as well as the area of the treatment areas, different machine brand and parameter in each treatment protocols. This is the main point that we need more researches in this treatment modality to confirm more specifically.

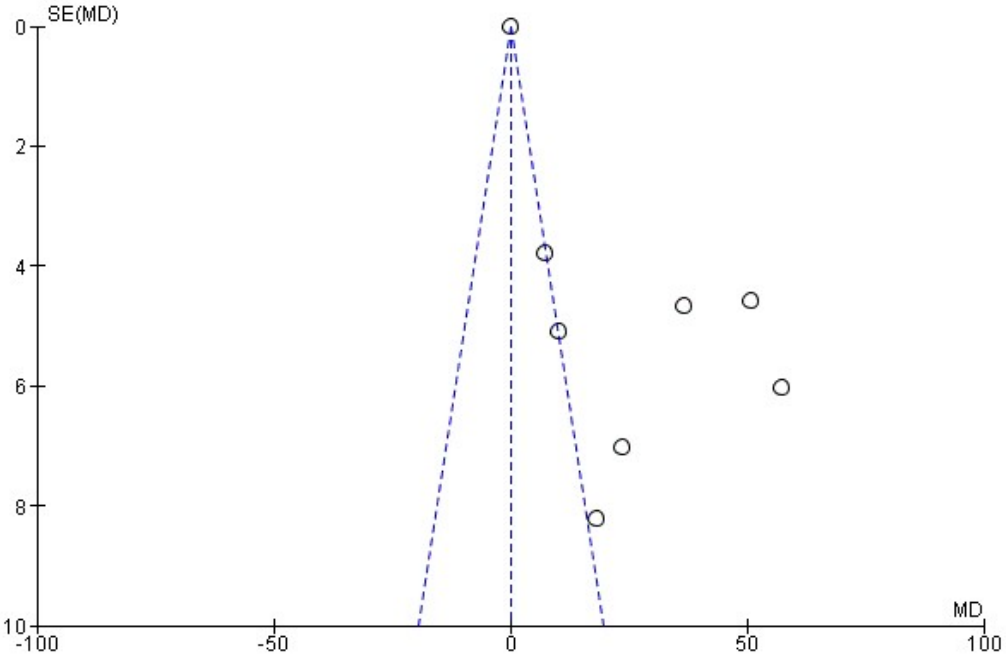

Figure 3 The funnel plot of studies on the hair density after the treatment in this meta-analysis

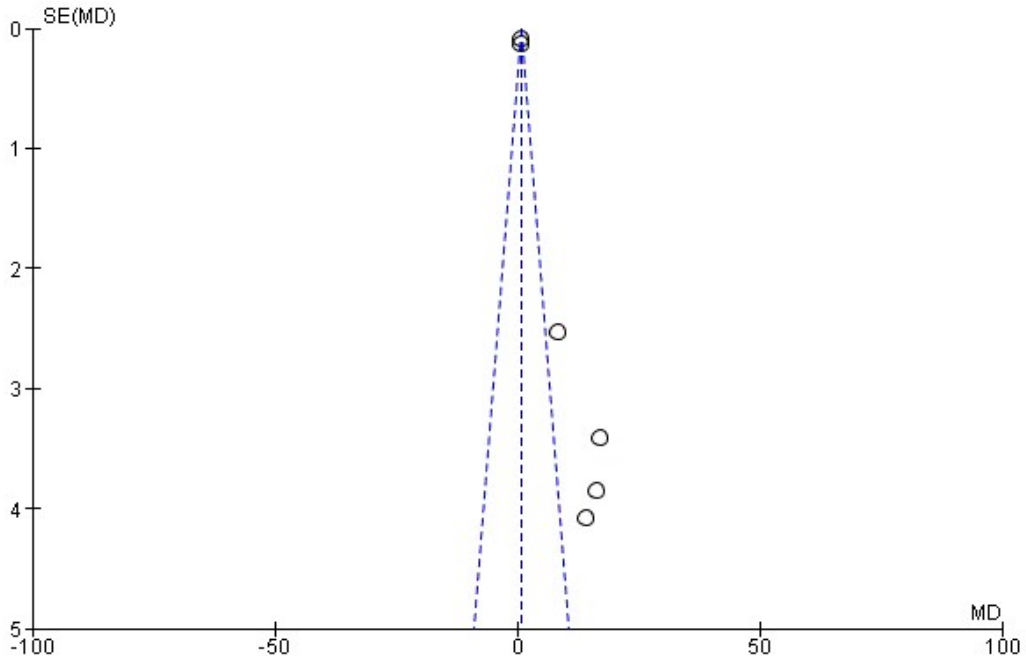

Figure 3 The funnel plot of studies on the hair shaft diameter after the treatment in this meta-analysis

6. Discussion

Using data from those four studies, our study was the first meta-analysis to estimate the efficacy of the 1550-nm Erbium glass fractional laser. In the present meta-analysis, we showed that the increasing the hair density as well as the hair shaft diameter was enlarger. The result was consistent in the analysis of an interventional study (hair density male IV=7.32, female IV=10.28; hair shaft diameter, male IV=0.72 and female IV=0.61), a prospective trial (hair density IV=57.00 and hair shaft diameter IV=17.00) (Alhattab et al, 2019). Another single center, semi-experimental study (the density of terminal hair IV=23.48, non- vellus hair IV=18.26, vellus:non-vellus IV=-0.05 and hair shaft diameter IV=8.22) (Meephansan et al, 2018) and a randomized, investigator-blinded, controlled, split-scalp study (the hair density of combination therapy IV= 0.54, monotherapy IV=36.52; hair shaft diameter of combination therapy IV=16.35 and monotherapy IV=14.16) (Suchonwanit et al, 2019). In addition, the results in each study showed high significant outcome in the mean of successful treatment, those results have a variation of positivity due to some studies focus more in female participants and another study included only male while other included both male and female which included more specific result in the density of vellus hair, non-vellus hair and the ratio of vellus to non- vellus hair.

Moreover, there was a study which was recruited only male patients which were AGA positive under the treatment of half scalp which mean a half of each patient received minoxidil solution 5% alone and another haft received 5% minoxidil together with 1550-nm Erbium glass fractional laser (Suchonwanit et al, 2019). The positive outcome variation could be also caused by different machine in each study and the parameter as well, the treatment of non-ablative fractional laser showed that in female have more significant result than male and it's also revealed that in the fronto-vertical presentation have better outcome, while the most resistant site was a bi-temporal recession and some studies they recruited different stages of AGA patient such as AGA

from stage II to IV, female pattern hair loss from stage II to III with the age range from 18 to 55 years old (Lee et al, 2011), while we already know that the treatment shows higher efficacy in younger age and started the treatment in earlier stages.

Fractional laser therapy may also be advantageous because it not only treats alopecia but may also prevent recurrent hair loss. Fractional lasers induce hair growth when restricted to appropriate settings by upregulating the Wnt/βcatenin pathways and efficiently penetrating the scalp. Although the exact mechanisms of certain fractional lasers on hair regrowth are not yet well understood, trauma stimulated wound healing likely plays a role. Hair follicle stem cells provide progeny that migrate to the epidermal defect and promote re-epithelialization. This cutaneous wound healing process increases tremendously during the anagen stage of the hair cycle, and additional hair follicles regrow after wounding. Combination therapy with agents such as minoxidil may produce a synergistic effect in stimulating hair growth. Human and animal studies have suggested the effectiveness and safety of the 1550-nm fractional Erbium-glass laser.

No significant adverse effects during treatment had been noticed. Some patient developed mild erosion after treatments without sequelae; and other few patients reported mild erythema resolved spontaneously within 1 day, and some also reported burning sensation in the treated area that resolved within hours.

In sum, the overall of the studies was 25.26 (95% confidence interval CI 8.62 to 41.89). In the other hand, the change in hair shaft diameter, the overall SMD was 2.03 (95% confidence interval CI 0.91 to 22, 14) (fig.2). The result indicated the significant increase in hair density (overall P=0.003, I2=98%) and hair shaft diameter (overall P=0.0004, I2=92%).

7. Conclusion

In conclusion, the use of 1550-nm Erbium glass non-ablative fractional laser is an effective treatment to embrace for use in the treatment of androgenic alopecia, it's fully utilized that can be a better choice for those patients who desired to use an alternative treatment beside some available medical therapy due to the side effects and LLLT device is a bit pricy as well as the complication if hair transplantation. Many of the results has shown in this study that there is an overall improvement in hair regrowth in both hair shaft diameter and hair density. Since the 1550-nm Erbium glass fractional laser is the new treatment provided very good outcome with minimal side effects. Lastly, more extensive research needs to be done in this treatment to help determine which patients such as male, female and differentiation in the age rang are the ideal for this type of treatment and those which are ideal for the alternative treatment.

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