Study of US FDA Clearance Home-Use Low Level Light/Laser Therapy for Androgenetic Alopecia

Poom Visutjindaporn[1], Yardnapar Parcharoen[2], and Suparuj Lueangarun[1*]

[1]Division of Dermatology, Chulabhorn International College of Medicine, Thammasat University, Pathum Thani, Thailand
[2]Chulabhorn International College of Medicine, Thammasat University, Pathum Thani, Thailand
[*]Corresponding author, E-mail: saoraya180@gmail.com

Abstract

In vivo and in vitro studies proved that Low level light/laser therapy (LLLT) could stimulate hair growth. Nowadays there are a lot of home-use low level light therapy devices sold in the USA. However, not all of them are cleared by the US Federal Drug Administration. The purpose of this study was to evaluate the low level and light therapy technology in the treatment of pattern hair loss and the articles published in PubMed relating to the US FDA cleared LLLT devices. To assess the low-level light therapy technology, we identified the commercially available home-use low level light therapy devices cleared by the US FDA by searching the FDA 510(K) Premarket Notification database. We also identified the articles published in PubMed to support these devices. Only fourteen devices were included in the study and compared. The home-use LLLT device varied in shape, light sources, the number of diodes, wavelength, total power, and price. Only eight articles that supported the devices were found in PubMed. Of these, six articles are RCTs and two articles are cohort studies. All of the studies were conducted by recruiting patients who have mild to moderate pattern hair loss with not more than 26-week duration. No head-to-head study is conducted to compare the efficacy of these LLLT devices at this moment. Therefore, in the future, the study of their efficacies should be conducted in long term follow up; include the severe pattern hair loss patients and compare between these devices.

Keywords: *Low level light therapy, Low level laser therapy, Photobiomodulation, Pattern hair loss, Androgenetic alopecia, Hair growth*

1. Introduction

Pattern hair loss (PHL), also called androgenetic alopecia (AGA), is still the main problem depriving the self-esteem of people of both sexes. AGA affects half of the men by age 50, while more than half of women aged over 80 have female pattern hair loss (Gan & Sinclair, 2005). Although pattern hair loss cannot cause fatal, many patients lose their confidence and become stressful.

The current treatments for this disease approved by the FDA are topical minoxidil, which has various forms including solution, foam, and shampoo and oral finasteride. These drugs normally provide a beneficial result. Nevertheless, oral finasteride has some unfavorable effects including erectile dysfunction, a decrease of libido, and an increase of body hair growth. Therefore, patients who have poor responses or people who get unwanted side effects need alternative treatment choices.

In 1967, Mester, Szende, and Tota (1967) did research on mice by using the ruby laser. Surprisingly, the laser increased hair growth on the shaved-off area of the animals' backs instead of producing cancer. This was the first display of "photobiostimulation" or low-level laser therapy (LLLT). Since then, LLLT has been studied by many scientists. Nowadays, the utilization of LLLT is adapted to many people all over the world for many medical conditions especially in skin diseases including AGA.

The theory of the mechanism of LLLT is that LLLT stimulates the mitochondria located in the hair bulge stem cells. Cytochrome c oxidase (CCO) in the membrane of mitochondria is the target chromophore of red light leading to mitochondrial respiration. ROS and ATP released stimulate cellular proliferation, migration, and oxygenation which consequently stimulate hair growth (Hamblin, 2019).

In 2007, there was the first cleared a LLLT device for male pattern hair loss by the United States Food and Drug Administration (FDA). Since then, many manufacturers have adapted LLLT technology and created LLLT devices. Because manufacturers aim to provide users with a convenient and user-friendly

experience, the LLLT devices in the current market have many forms. Nevertheless, only some of them are cleared by the FDA and there are only some products that have articles published to support their efficacy. In this review, we will evaluate the low level and light therapy technology in the treatment of pattern hair loss and the articles published in PubMed relating to the US FDA cleared LLLT devices.

2. Objectives

1. To assess the low level light therapy technology in terms of LLLT device for the patients with androgenetic alopecia
2. To identify the commercially available home-use LLLT devices cleared by the US FDA
3. To identify the articles published in PubMed to support LLLT devices cleared by the US FDA
4. To identify device design, features and existing clinical evidence

3. Methods

To identify the devices, a search using product code "OAP" from the FDA 510(k) Premarket Notification database for all home-use low level light therapy devices was done. A 510(K) shows that the device sold is at least as unharmed and effective, that is, substantially equal, to a legally marketed device. OAP is the code for the device categorized as "laser, comb, hair" intended to promote hair growth. Afterwards, the identification of all devices which can be purchased in the USA was conducted by combining and reviewing the aforementioned data with the information showed on the websites of manufacturers.

To identify the articles related to the device, a search of PubMed was conducted on November 15, 2019. A search strategy was (low level light therapy OR low-level laser therapy OR photobiomodulation OR hairmax lasercomb) AND (androgenetic alopecia OR female pattern hair loss OR male pattern hair loss OR pattern hair loss OR hair growth). The inclusion criteria included (1) studies on AGA or FPHL (2) human studies (3) studies that use US-FDA cleared devices. Exclusion criteria included (1) review articles (2) studies that use other modalities (3) animal studies (4) articles not written in English. Only eight studies met the requirements above and were included in this review. See Figure 1.

Proceedings of RSU International Research Conference (2020)

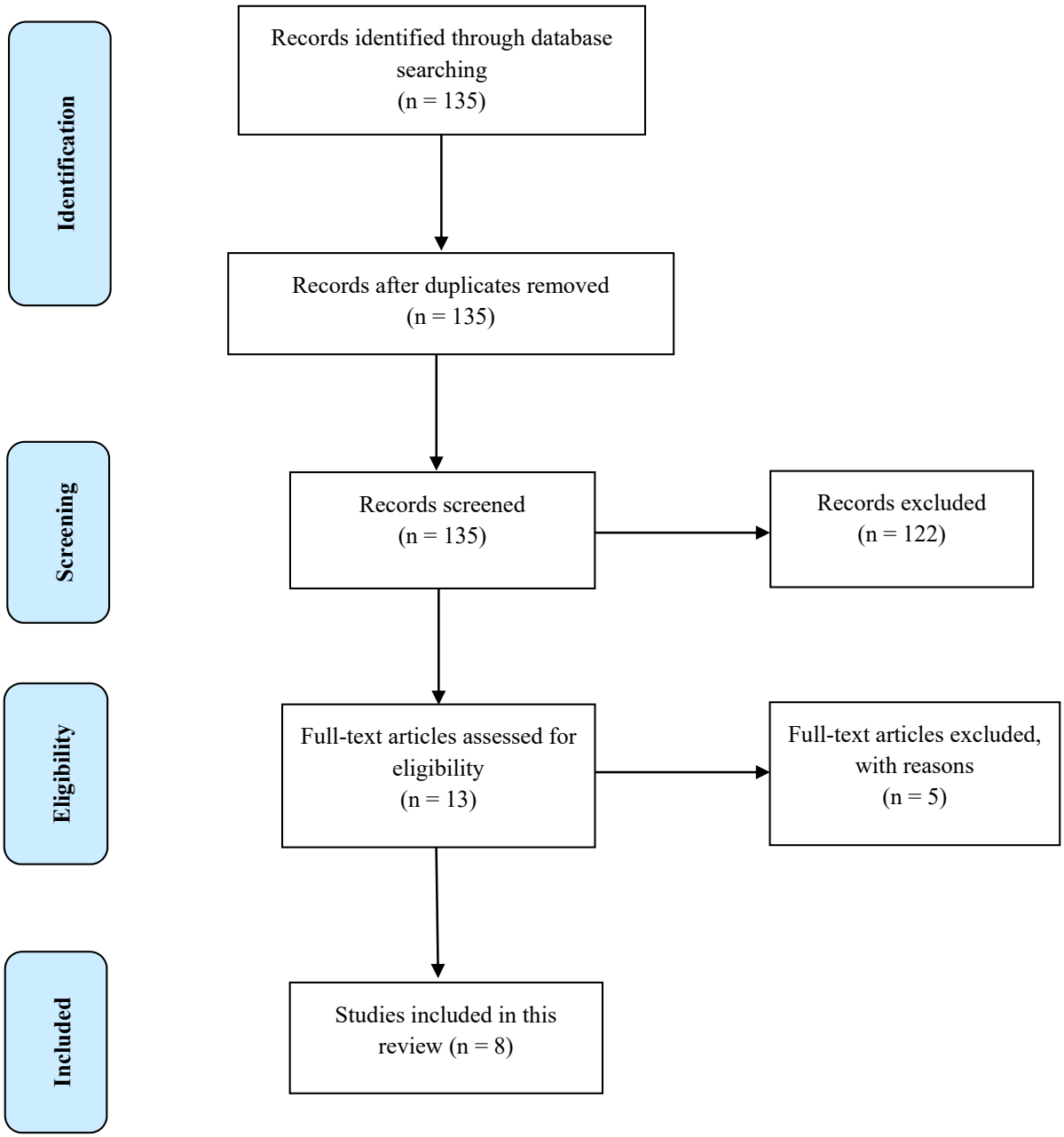

Figure 1 Search method

4. Results and Discussion

4.1 Results

Devices

There were 58 entries in the FDA 510(k) Premarket Notification medical device database. Of these, 14 home- use low level light therapy devices were sold in the USA at the time of this writing. The Characteristics of the 14 devices were summarized in Table 1.

Table 1 Summary of LLLT devices cleared by the US FDA

	Capillus 82	**Capillus 202**	**Capillus 272**
Shape	Sports cap	Sports cap	Sports cap
Laser diode quantity/Wavelength	82/650	202/650	272/650
Light emitting diode quantity/Wavelength	-	-	-
Power/diode	≤ 5mW	≤ 5mW	≤ 5mW
Total power output	≤ 410mW	≤ 1010mW	≤ 1360mW
Treatment regimen	30 mins	30 mins	30 mins
Frequency	3-4 times/week	3-4 times/week	3-4 times/week
Price (US$)	799	1999	3000
Sample size	-	-	44 F
Duration of study	-	-	17 weeks
Outcome	-	-	A 51% increase in terminal hair counts as compared with sham-treated control patients

Table 1 (Continue) Summary of LLLT devices cleared by the US FDA

	HairMax Lasercomb 7	**HairMax Lasercomb 9**		**HairMax Lasercomb 12**
Shape	Comb	Comb		Comb
Laser diode quantity/Wavelength	7/655	9/655		12/655
Light emitting diode quantity/Wavelength	-	-		-
Power/diode	≤ 5mW	≤ 5mW		≤ 5mW
Total power output	≤ 35mW	≤ 45mW		≤ 60mW
Treatment regimen	15 mins	11 mins		8 mins
Frequency	3 times/week	3 times/week		3 times/week
Price (US$)	295	395		495
Sample size	7 F 28 M	110 M	21 F 11 M	141 F 128 M
Duration of study	Cohort 6 mo	26 weeks	Cohort 2 yr	26 weeks
Outcome	Total hair counts increased by 93.5% and total hair tensile strength increased by 78.9%	Mean terminal hair density increased by 19.8 hairs/cm2	8 with significant improvement, 20 with moderate improvement, 4 with no improvement	Overall, terminal hair density increased by 15.27 hairs/cm2

Table 1 (Continue) Summary of LLLT devices cleared by the US FDA

	HairMax LaserBand 41	HairMax LaserBand 82	Regrow 272 by HairMax
Shape	Headband	Headband	Sports cap
Laser diode quantity/Wavelength	41/655	82/655	272/655
Light emitting diode quantity/Wavelength	-	-	-
Power/diode	≤ 5mW	≤ 5mW	≤ 5mW
Total power output	≤ 205mW	≤ 410mW	≤ 1360mW
Treatment regimen	3 mins	90 secs	30 mins
Frequency	3 times/week	3 times/week	3 times/week
Price (US$)	595	795	999
Sample size	-	-	-
Duration of study	-	-	-
Outcome	-	-	-

Table 1 (Continue) Summary of LLLT devices cleared by the US FDA

			iGrow
Shape			Helmet
Laser diode quantity/Wavelength			21/655
Light emitting diode quantity/Wavelength			30/655
Power/diode			≤ 5mW
Total power output			≤ 255mW
Treatment regimen			25 mins
Frequency			Every other day
Price (US$)			695
Sample size	44 M	47 F	45 F
Duration of study	16 weeks	16 weeks	16 weeks
Outcome	35% increase of in terminal hair count	37% increase of in terminal hair count	Average hair density of 207+-12.97/cm2

Table 1 (Continue) Summary of LLLT devices cleared by the US FDA

	iRestore	LaserCap LCPRO	Nutrastim Laser Hair Comb
Shape	Helmet	Sports cap	Comb
Laser diode quantity/Wavelength	21/650	224/650	12/655
Light emitting diode quantity/Wavelength	30/660	-	-
Power/diode	≤ 5mW	≤ 5mW	≤ 5mW
Total power output	≤ 255mW	≤ 1120mW	≤ 60mW
Treatment regimen	25 mins	36 mins	8 mins
Frequency	Every other day	Every other day	3 times/week
Price (US$)	595	3000	279
Sample size	-	-	-
Duration of study	-	-	-
Outcome	-	-	-

Table 1 (Continue) Summary of LLLT devices cleared by the US FDA

	Theradome LH 80 PRO
Shape	Helmet
Laser diode quantity/Wavelength	80/678
Light emitting diode quantity/Wavelength	-
Power/diode	≤ 5mW
Total power output	≤ 400mW
Treatment regimen	20 mins
Frequency	2 times/week
Price (US$)	895
Sample size	-
Duration of study	-
Outcome	-

Overall, there were four major shapes of the devices including sports cap (5 devices), headband (2 devices), comb (4 devices), and helmet (3 devices) depending on the manufacturers. Each device had its own number of light sources. Of these, two devices which were iGrow® and iRestore® contained both laser diodes and light emitting diodes. 12 of the devices contained only laser diodes ranging from 7 to 272 diodes and the median is 81 laser diodes. All of these devices contained laser diodes with a power that no more than five mill watts (mW) per diode. However, the total output of the devices ranged from approximately 35 to 1360 mW (The median is 405 mW). In term of a wavelength, there were five devices that had a wavelength of 650 nm and eight devices that had a wavelength of 655 nm. Theradome® LH 80 Pro was the only device that emits the wavelength at 678 nm. The treatment regimens were ranging from 90 secs to 36 mins depending on the shapes and total power output. HairMax® LaserBand 82 required the least treatment time which was 90 secs. On the other hand, LaserCap® LCPRO required the most at 36 mins. There were three major frequents to use the devices: 3-4 times a week, 3 times a week, and every other day. The retail cost started from $279 to $3000. However, the more numbers of diodes they contained, the more expensive they were.

Clinical Trials

Only some of 14 devices had published documents supporting their efficacy. A few of them had supporting clinical trials which were not published in the journals. 135 articles were obtained after initial searches. The removal of 122 articles was done after a screening of titles and abstracts. A total of 14 articles were chosen for full-text review. Only 8 articles were included in this study.

In summary, there were 6 randomized control trials: one for Capillus®, two for HairMax®, and three for iGrow® and also 2 cohort studies: one prospective cohort study by Satino and Markou (2003) and one retrospective cohort study by Munck, Gavazzoni, and Trueb (2014) published in PubMed to support the devices. Of these RCTs, there were 3 articles studied in only women including Friedman and Schnoor (2017), Lanzafame et al. (2014), and Esmat et al. (2017) and also 2 articles studied in only men including Leavitt et al. (2009), and Lanzafame et al. (2013). Study from Jimenez et al. (2014) was the only RCT conducted in both sexes and had the largest number of participants (128 males and 141 females). On the contrary, the rest had small sample sizes. The participants included in most RCTs had mild to moderate PHL (Norwood-Hamilton class IIa-V for men and Ludwig–Savin Baldness Scale I-2, I-3, I-4, II-1, II-2 for women). The duration of studies ranged from 16 weeks to 26 weeks (The mean was 19.5 weeks). For the assessment, the majority of RCTs examined in these articles showed positive results which were hair regrowth. Most of the LLLT treatment groups showed statistically significant improvement in hair count compared with the control group. In two non-controlled trials, LLLT also showed improvement in comparison with a baseline without P-value provided.

4.2 Discussion

There are 14 home-use low level light therapy devices cleared by FDA in the current US market. The primary differences are shape, price, light source, the number of diodes, wavelength and total power output. Since there is no head-to-head study to evaluate devices, it is unable to know whether which one offers a clinical benefit over another. Considering the number of diodes, combs use the least number of diodes ranging from 7 to 12 diodes. The prices of combs are cheaper than the other shapes, so they are good options for patients who have financial limitations. Leavitt et al. (2009) and Jimenez et al. (2014) also proved the clinical efficacy by using the HairMax Lasercomb®. The hand-free devices including caps and helmets usually use the high number of diodes ranging from 51 to 272 diodes offer user-friendly ability. Patients can do their daily activities during the treatment session. However, the price is higher than the other devices. Friedman and Schnoor (2017) proved the efficacy of Capillus® 272 caps. Similarly, Lanzafame et al. (2013), Lanzafame et al. (2014) and Esmat et al. (2017) showed the benefits of the iGrow® helmet.

Among 14 devices, 12 of them are composed of only laser diodes. Scientists claimed that the coherence of the laser had more impact on chromophore. Nevertheless, some head-to-head studies comparing both light sources showed no difference in their effect. Considering the wavelength, we can see that all the devices use the light sources with 650 to 678 nm. That is because cytochrome c oxidase which is the chromophore for LLLT has an absorption peak at 660 nm (Karu et al., 1982).

According to Arndt-Schulz Law, it is widely accepted that if the irradiance or the duration is too short, there is no response. Similarly, if the irradiance or duration is too high, then the response may be inhibited instead. According to Huang et al. (2009), the irradiance of 2-4 J/cm^2 is suspected to be appropriate. When this theory applied to the LLLT device, we can observe that these LLLT devices usually provide patients with this therapeutic irradiance.

Considering the articles published supporting the devices, we can observe that the participants included in these articles are mild to moderate pattern hair loss. However, no study conducted in severe pattern hair loss which should be included in further study. In terms of duration of studies, no RCT conducted longer than 26 weeks is observed. Therefore, the long-term efficacy which is essential in the real setting has not been investigated yet. The duration of treatment depends on the power density of the device. If the device has a high-power density, the treatment duration will short. This is because when it comes to the irradiance (power multiply by duration time), it should be within therapeutic range (2-4 J/cm^2). Unfortunately, in RCTs

Proceedings of RSU International Research Conference (2020)

included in this study, only Friedman and Schnoor (2017), Lanzafame et al. (2013), and Lanzafame et al. (2014) showed the irradiance used in their methods.

The standard therapy including oral finasteride and topical minoxidil are used to compare the efficacy of LLLT. According to Roberts et al. (1999), 1 mg of finasteride could increase hair count 69 hairs in 5.1 cm^2 area at 6 months (13.5 hairs/cm^2) while the studies from Jimenez et al. (2014) and Leavitt et al. (2009) showed an increase in terminal hair density of 15.27 hair/cm^2 and 19.8 hair/cm^2, respectively. Similarly, the study from Olsen et al. (2002) also showed that 5% topical minoxidil could increase hair count 18.6 hairs/cm^2. Therefore, the efficacy of LLLT appeared to be comparable to conventional pattern hair loss treatments. This similar efficacy was shown in Esmat et al. (2017). However, it was observed that combination therapy was more effective.

5. Conclusion

Nowadays, there are many home-use LLLT devices in the current US market. Only 14 devices cleared by the US Federal Drug Administration which divide into four main categories; cap, comb, hairband, and helmet. The light sources are depending on the manufacturers. However, the laser diode is more popular than light emitting diode. The wavelength is within the range of 650-678 nm. Only 8 articles published to support the device (2 cohort studies, 6 RCTs). These prove the promising efficacy of the LLLT devices. However, the durations of these studies are fewer than 26 weeks. Therefore, in the future, these devices should be evaluated in the long term (at least 1-2 years) and also in patients with severe PHL. Moreover, to compare the efficacy among them, a head-to-head study should be conducted.

6. Acknowledgements

The author gratefully acknowledges the financial support provided by the National Research Council of Thailand (NRCT) under the FY2020 Thesis Grant for Master Degree Student.

7. References

Esmat, S. M., Hegazy, R. A., Gawdat, H. I., Abdel Hay, R. M., Allam, R. S., El Naggar, R., & Moneib, H. (2017). Low level light-minoxidil 5% combination versus either therapeutic modality alone in management of female patterned hair loss: A randomized controlled study. *Lasers in surgery and medicine, 49*(9), 835-843.

Friedman, S., & Schnoor, P. (2017). Novel approach to treating androgenetic alopecia in females with photobiomodulation (low-level laser therapy). *Dermatologic Surgery, 43*(6), 856-867.

Gan, D. C., & Sinclair, R. D. (2005). *Prevalence of male and female pattern hair loss in Maryborough.* Paper presented at the Journal of Investigative Dermatology Symposium Proceedings.

Hamblin, M. R. (2019). Photobiomodulation for the management of alopecia: mechanisms of action, patient selection and perspectives. *Clinical, cosmetic and investigational dermatology, 12*, 669.

Huang, Y.-Y., Chen, A. C.-H., Carroll, J. D., & Hamblin, M. R. (2009). Biphasic dose response in low level light therapy. *Dose-response, 7*(4), 09-027.

Jimenez, J. J., Wikramanayake, T. C., Bergfeld, W., Hordinsky, M., Hickman, J. G., Hamblin, M. R., & Schachner, L. A. (2014). Efficacy and safety of a low-level laser device in the treatment of male and female pattern hair loss: a multicenter, randomized, sham device-controlled, double-blind study. *American journal of clinical dermatology, 15*(2), 115-127.

Karu, T., Kalendo, G., Letokhov, V., & Lobko, V. (1982). Biostimulation of HeLa cells by low-intensity visible light. *Il Nuovo Cimento D, 1*(6), 828-840.

Lanzafame, R. J., Blanche, R. R., Bodian, A. B., Chiacchierini, R. P., Fernandez-Obregon, A., & Kazmirek, E. R. (2013). The growth of human scalp hair mediated by visible red light laser and LED sources in males. *Lasers in Surgery and Medicine, 45*(8), 487-495.

Lanzafame, R. J., Blanche, R. R., Chiacchierini, R. P., Kazmirek, E. R., & Sklar, J. A. (2014). The growth of human scalp hair in females using visible red light laser and LED sources. *Lasers in Surgery and Medicine, 46*(8), 601-607.

Leavitt, M., Charles, G., Heyman, E., & Michaels, D. (2009). HairMax LaserComb® laser phototherapy device in the treatment of male androgenetic alopecia. *Clinical drug investigation, 29*(5), 283-292.

Mester, E., Szende, B., & Tota, J. (1967). Effect of laser on hair growth of mice. *Kiserl Orvostud, 19*, 628-631.

Olsen, E. A., Dunlap, F. E., Funicella, T., Koperski, J. A., Swinehart, J. M., Tschen, E. H., & Trancik, R. J. (2002). A randomized clinical trial of 5% topical minoxidil versus 2% topical minoxidil and placebo in the treatment of androgenetic alopecia in men. *Journal of the American Academy of Dermatology, 47*(3), 377-385.