JOURNAL OF COSMETIC AND LASER THERAPY
2018, VOL. 20, NO. 3, 140–144
https://doi.org/10.1080/14764172.2017.1376099

Laser-assisted hair removal for facial hirsutism in women: A review of evidence

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ABSTRACT

Poly cystic ovarian syndrome (PCOS) has been described as the common diagnosis for hirsutism in women. Facial hirsutism is by far the most distressing symptom of hyperandrogenism in women with PCOS. A statistically significant improvement in psychological well-being has been reported in patients with PCOS allocated for laser-assisted hair removal. The theory of selective photothermolysis has revolutionized laser hair removal in that it is effective and safe, when operated by sufficiently trained and experienced professionals. Long-pulsed ruby (694 nm), long-pulsed alexandrite (755 nm), diode (800–980 nm), and long-pulsed Nd:YAG (1064 nm) are commercially available laser devices for hair removal most widely studied. This article will introduce the fundamentals and mechanism of action of lasers in hair removal, in a contemporary literature review looking at medium to long term efficacy and safety profiles of various laser hair removal modalities most widely commercially available to date.

ARTICLE HISTORY
Received 13 June 2017
Accepted 1 September 2017

KEYWORDS
Lasers and light sources; long-pulsed lasers; laser-assisted hair removal; PCOS

Introduction

Until the beginning of the decade, the definition of Polycystic Ovary Syndrome (PCOS) has been a subject of debate. In 2006, the Androgen Excess Society (AES) set up a taskforce to re-define the syndrome based on evidence in published peer-reviewed literature and a consensus reached and critiqued amongst experts in the field (1). The take force recommended a diagnostic criteria for the PCOS to comprise the presence of ovulatory disorder, and/or clinical or biochemical evidence of hyperandrogenism, in the absence of a known disorder to explain the collection of signs and symptoms. Amongst clinical signs of PCOS, hirsutism appears to be the most distressing symptom, to account for one of the most common reasons for seeking hair removal that is only very rarely funded by the UK National Health Service (NHS) (2). In spite of the demand, there is little high quality research evidence on the use of lasers in the treatment of facial hirsutism. A randomized controlled trial found an improvement in self-reported psychological morbidity at 6 months in the intervention group treated with Alexandrite laser (Apogee 6200; Cynosure, Chelmsford, MA, USA; 755 nm, 20 ms, spot size 12.5 mm) (2). Individuals randomly allocated for treatment on the face, in comparison with the control group who received ineffective treatment. Operators were aware of the allocation and were therefore un-blinded. Whilst the study was the most relevant to laser hair removal for facial hirsutism associated with androgen excess to date, it did not provide objective data on the effectiveness of treatment. Subjective outcomes included self-reported time spent on hair removal were used to assess disease severity post intervention, in addition to the psychological impact of facial hirsutism measured on validated scoring tools for depression and anxiety.

Mechanism of action of lasers

Light amplification by stimulated emission of radiation, otherwise widely known by the acronym LASER, is a light source that emits energy within a certain portion of the electromagnetic (EMR) spectrum. In clinical practice, laser wavelengths can be categorized into 200–400 nm ultraviolet (UV), 400–760 nm visible light (VIS), 760–1400 nm near-infrared (NIR), 1400–3000 nm mid-infrared (MIR), and longer wavelengths in the far-infrared (FIR) range (3). Laser light is distinctive to other light sources as it possess the following properties: 1. Laser light is **monochromatic** – it is a single color light, and therefore of a single wavelength; 2. Laser light has **narrow beam divergence**, measured in milli-radian (rad); 3. Laser light is **coherent**, which means light waves proceed in phase, both in space and in time. A laser device emits energy from a light source (usually a xenon lamp) into a medium (the laser rod), which could be solid, liquid, or gas confined in a chamber, where pockets of energy propagates before the escape through a partially reflecting mirror or unidirectional slit exit as an intensified beam. Laser-Tissue Interaction is the mechanism of action of laser on tissues – in the case of Laser Hair Removal, the photo-thermal interaction between laser and hair follicle. This is selective photothermolysis (4).

Judging by the chromophore's absorption co-efficient alone (Figure 1), the frequency-doubled 532 nm Nd:YAG lasers would have been the perfect choice to target follicular melanin in an over-simplified principle, but hair follicles are buried in the dermis, protected by the scatter of light, and the competing melanin in the epidermis, within the hair shaft and outer root sheath could reduce the effective fluence on the

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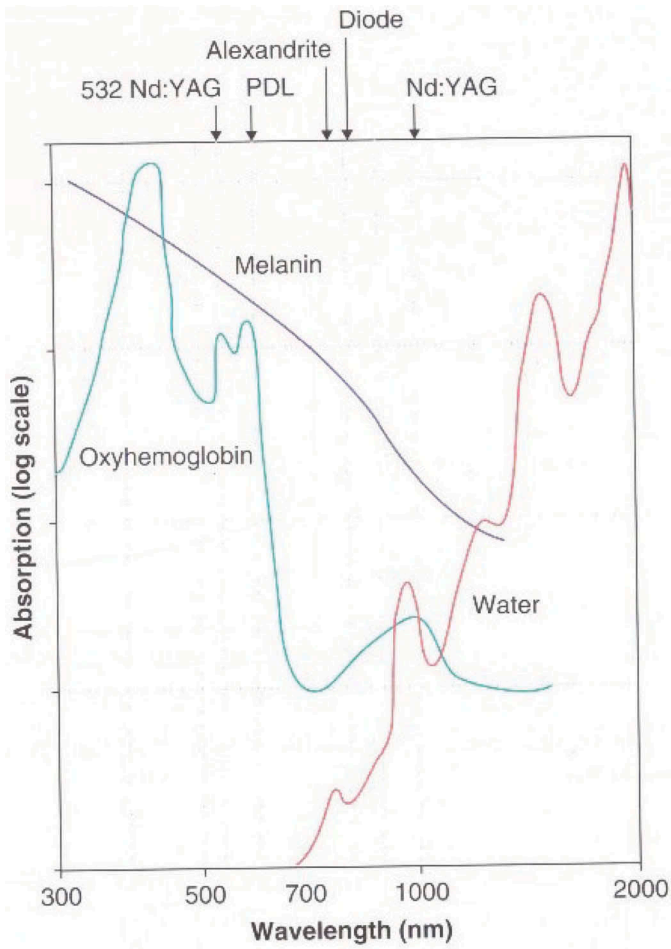

Figure 1. copyright and permission obtained from EV ross, scanned from *lasers and energy devices for the skin* (2^{nd} ed.) (5). Shorter wavelengths are preferentially absorbed by melanin; hence the risk of laser induced epidermal injuries, being highest in darker skin photo-types (IV–VI). Longer wavelengths penetrate deeper into the skin and minimize interaction with epidermal melanin, but require the compensation of higher fluences to fulfill effective photothermal damage of the target.

hair follicle and attenuate selective damage. It follows that laser hair removal has to utilize more than the theory of selective photothermolysis, originally coined by Anderson and Parish in 1983 (4). The effect of one single treatment with 0.27 ms, 694 nm ruby laser in 13 individuals has been described in a small, prospective observational study (6). In the study hair growth delay was apparent in all 13 study subjects with a reduction in terminal to vellus-like hair ratio in the treatment group.

The fundamental theory of selective photothermolysis had to be modified to accommodate the complexity of targeting a reservoir of stem cells in the hair bulge, which is responsible for hair regrowth and regeneration of skin and adnexal structures, in achieving permanent hair-removal (7); The theory of selective photothermolysis, originally coined by Anderson and Parrish in 1983, necessitates a targeted structure being abundant in a chromophore that corresponds with a specific **wavelength** of electromagnetic radiation (EMR) within the absorption spectrum (4,8). Three skin chromophores are of interest: oxyhemoglobin in blood, melanin in pigmented structures, and water that make up of 65% of tissue content. Permanent hair loss requires destruction of the hair bulge, which possesses no effective chromophore for the absorption of red/near-infrared radiation. It follows that energy has to be absorbed from its nearby melanin-bearing structures to achieve photothermolysis by heat diffusion, akin to the process of photocoagulation by targeting oxyhemoglobin in red blood cells, to induce diffusion of heat to the wall of blood vessels when treating port wine stains (9). The **pulse duration** must be significantly longer than the Thermal Relaxation Time (TRT), to achieve irreversible target (hair bulge) damage with maximum sparing of surrounding tissues. This is thermal damage time (TDT) (10). **Fluence**, the density of energy delivered in J/cm2 measured on skin surface, must be set to deliver maximum damage but minimum adverse side effects. In practice, the effective fluence destined for absorption is far less than that prescribed, owing to scattering as beams travel through a depth of tissue into the target. Increasing **spot size** of a laser beam increases effective fluence by compensating for scatter phenomenon (11). Lastly, surface cooling permits the use of higher fluences by reducing thermal injury to the epidermis, which is high in melanin content in pigmented skin-types and thus competing energy absorption.

The optimal device variables have not been established; Eremia et al. reviewed 89 cases retrospectively over a 4 year period treated with 755 nm alexandrite laser for hair removal in various body sites (face, extremities, axillae, pubis, and trunk), and found treatment effectiveness correlating positively with higher fluences, delivered in larger spot sizes (12–15 mm) in four to five treatments (12). The study bears very little information about patient's co-morbidities and current medication being taken, which could influence outcome. Polycystic ovary syndrome (PCOS) is associated with insulin resistance and metformin is an antiandrogen therapy for hirsutism in PCOS (13). Co-founding factors such as device settings and the number of treatments aside, the highest hair reduction at 6 months was achieved (79%) in skin photo-type I (14); lower (60%) amongst skin type V (15), and lowest in the presence of PCOS (31%) (16). A direct comparison between any two study outcomes is not possible owing to the lack of standardized treatment protocol in the former and un-controlled in the latter – the study conditions are different.

Patient assessment

Although hair removal with lasers is regarded as safe, all reports are based on subjects carefully selected to receive treatments that have been tailored to their skin photo-types. Patients must be given realistic expectations and an informed consent comprising understanding of potential risks is paramount. A complete medical history has to be evaluated to identify patients with pre-existing photosensitive or photo aggravated skin conditions, or recurrent cutaneous infections that may require prophylactic medications prior to treatment, any current or past practice of hair removal, factors to indicate the propensity for keloid scarring, as well as clinical evidence for endocrine (hormonal) dysfunction. The current medication history should follow an assessment of risk of drugs on the photosensitivity of skin. Published recommendations are diverse owing to the lack of controlled trial and therefore evidence to support or deny laser treatment with co-existing medical and medication history (17). Guidance is based upon physicians' core knowledge of drug side effects and pathophysiology of diseases, in relation to their response to electromagnetic radiation (EMR) and skin healing.

Darker skin photo-types (IV–VI) are associated with higher incidence of adverse effects by long pulse ruby laser (18). First, a higher density of epidermal melanin intercepts laser beam by absorption, to promote unwanted epidermal heating and resultant injury. This could be blistering with the consequences of hypo and hyperpigmentation. Darker skin types thus promotes a higher attenuation of effective fluence by the unwanted absorption in the path of laser beam. Second, the incidence of paradoxical hypertrichosis after laser hair removal appears to be higher amongst individuals with darker skin photo-types in a single center, retrospective study of 489 cases. By comparing clinical photographs before and after a various number of laser treatment with alexandrite laser, three patients were selected for cases of hypertrichosis without any other known cause (19). These cases were compared with 50 randomly selected patients used as the control. The treatment settings, age, gender, and the number of sessions received before the onset of increased hair growth were un-standardized. Subsequent reports of paradoxical hypertrichosis failed to identify a plausible pathogenesis but an association with darker skin types (III–IV) and underlying hormonal conditions such as PCOS is seen (20).

Pre-procedural preparation may include topical application of local anesthesia with lidocaine/prilocaine (EMLA cream), lidocaine alone or any other amide/ester local anesthetic combination. The level of pain and thence the need for topical anesthesia appears to be directly proportional to the total amount of energy absorbed by skin tissue; a larger spot size compensates for the scatter of laser beam below the surface of skin to deliver higher effective fluences in tissue, whilst darker skin types absorb laser beam energy more readily to cause greater discomfort (15,21).

Laser devices, safety, and efficacy

Long-pulsed ruby (694 nm), long-pulsed alexandrite (755 nm), diode (800–980 nm), and long-pulsed Nd:YAG (1064 nm) are commercially available laser devices for hair removal most widely studied; i.e. evidence is at least based on a case-control study.

The 694 nm ruby laser was the first laser device used to test the unmodified theory of selective photothermolysis originally coined by Anderson and Parrish in 1983 (4). Any wavelength shorter than 800 nm is preferentially absorbed by melanin with a higher co-efficient than other competing chromophores, such as oxyhemoglobin and water. The ideal device has to be one with a wavelength that is preferentially absorbed by melanin, penetrates deep to reach the hair follicles, and have high enough effective fluence to overcome the scatter in dermis. With long-pulsed (3 ms) ruby laser, cessation of long term hair regrowth is possible in successive treatment sessions, with lesser hair density and a greater proportion of vellus hair on regrowth (22). A multicenter trial on 200 patients with skin phototypes I–V demonstrated long-term clinical effectiveness with very few adverse effects, of which none was permanent (23). Nevertheless, the few participants with darker skintypes (III–V) were treated with far lower fluences and no more than 4 sessions – the treatment protocol was tailored individually by altering device settings to minimize adverse effects – darker skintypes are prone to adverse effects owing to the unwanted preferential absorption of light by epidermal melanin, to cause tissue injury.

Adverse effects of laser hair removal have only come under review in large scale since the start of this century. 480 cases of laser hair removal were reviewed in a retrospective, multicenter study for adverse effects over a 3 month period (18). Lasercare (Sk:N) clinics ltd. operate under the authority of Care Quality Commission. Lasers devices used in the study included long-pulsed Ruby (694 nm Lambda, UK), long-pulsed alexandrite (755 nm LPIR, Cynosure, Chemsford; Gentlelas, Candela, Wayland, MA; Apogee, Cynosure) and long-pulsed Nd:YAG (1064 Lyra, Laserscope, San jose, CA). The study has shown very few cases of long term adverse effects and the more serious side effects occur when dark skin types were treated with the ruby laser. This correlated well with the core knowledge and understanding of shorter wavelengths having a greater absorption coefficient for competing epidermal melanin; hence a greater incidence of epidermal injury with blistering and post inflammatory pigmentary changes. Side effects included blistering, hyper and hypopigmentation, and thrombophlebitis and atrophic scarring only in two exceptional cases (Figure 2). Incidence of adverse effects were highest in skin types III to V; higher with the use of long-pulsed ruby laser in darker skin types in comparison to other devices. Long-pulsed Nd:YAG laser hair removal appears safest in pigmented skin.

Twenty women with skin photo-types IV to VI took part in a non-randomized study to supplement the safety profile of long-pulsed Nd:YAG (1062 nm Lyra, LaserScope, San Jose,

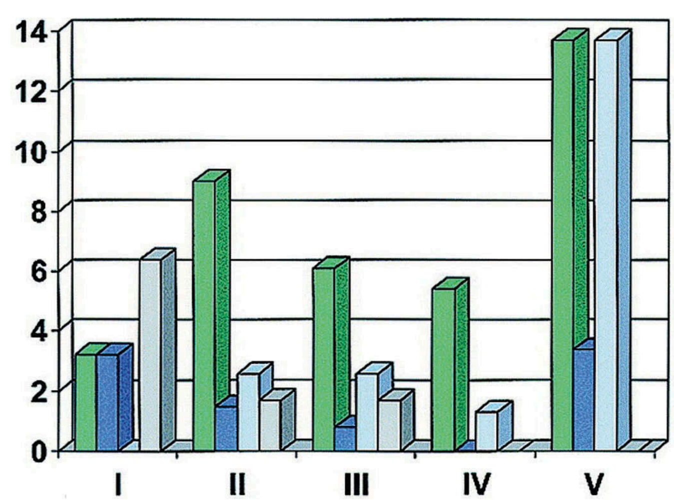

Figure 2. copyright Lanigan 2003 (18). Observed side effects in 480 patients receiving at least one laser hair removal treatment included blistering (green), hypopigmentation (dark blue), hyperpigmentation (light blue), and scabbing (gray). Mean durations range from 2 days in scabbing, to 120 days in hypopigmentation. One case of atrophic scarring and thrombophlebitis were considered to be exceptional circumstances and therefore have doubtful relevance to laser treatment. There is currently no data to categorize anatomical sites against the risk of adverse effects of laser hair removal.

CA) laser treatment (24). This was the first prospective study of its kind to demonstrate histological evidence of selective follicular destruction and a prolonged reduction in hair regrowth after three laser treatments at 6 months, with an extended period of post-procedural evaluation of clinical hair reduction of 12 months. Adverse effects were universally temporary, mirroring the observation by Lanigan in 2003 (18). The validity of the study has been offset by the lack of control, and un-randomized selection of subjects could result in selection bias. None of the study subjects appeared to have any underlying medical condition relevant to hirsutism such as polycystic ovarian syndrome (PCOS); there is currently no data available for photo-epilation with long-pulsed Nd:YAG laser amongst hirsute women with PCOS.

Alexandrite laser has been proven to be at least just as effective and safe in hair reduction in a double blinded, randomized trial on 15 individuals of skin photo-types III and IV (25). In this study the long pulsed 755 nm alexandrite laser was given in 4 sessions at 8 week intervals, in two groups of different spot sizes (12 and 18 mm), to compare against long pulsed 1064 nm Nd:YAG laser as well as two lasers in combination. Both alexandrite and Nd:YAG lasers result in 75.9% of hair reduction when delivered in long-pulse (3 ms), 84.3% with alexandrite laser in a larger spot size (18 mm), and apparently no added benefit from combining treatments. In fact, incidence of temporary hyperpigmentation tended to be higher in combination therapy. The authors did not report any other side effects despite having one patient dropping out of the study owing to adverse reaction. Hair density is variable amongst individuals; pre-treatment hair density and the type of hair (terminal, vellus) within the small, standardized 1 cm^2 test zone would have made an impact on response to treatment. There is sampling bias – the smaller the surface area of the test zone the bigger the bias. The study is also not relevant to individuals suffering from PCOS-related facial hirsutism, again because of the lack of reference of the disorder as well as the seemingly too high percentage hair reduction for individuals with PCOS. 755 nm alexandrite laser hair removal has been reported as safe for Fitzpatrick skin types IV–VI in a small, prospective case series of 150 patients receiving one treatment session in one or more anatomical locations (15). The starting fluence was said to be an arbitrary 16 J/cm^2, which was adjusted based on clinical response. Whether a clinical end point was reached or erythema was too diffuse to warrant reduction of fluence was up to one's interpretation. Adverse effects included blistering, folliculitis, and transient hypo and hyperpigmentation without scarring – both cases of pigmentary changes resulted from blistering in skin type VI.

The long-pulsed 800 nm diode laser demonstrated efficacy for long-term hair removal comparable to alexandrite laser in a 12-month, randomized, split-side comparative study of 15 individuals of skin phototypes I–V (14). No statistical difference was found in this comparison, with the highest reduction of 95% at one-year follow up. Both devices were tested with inconsistent variables to reach clinical end points (perifollicular erythema and oedema). Whilst the 'ideal' laser-device variables remain obscure, darker skin types could only tolerate low fluences in the range of 10–12 J/cm^2 for effective long-term laser hair removal (14,15,24). Combination therapy with long-pulsed 755 nm alexandrite laser and 800 nm diode laser in a 37 year old woman with underlying polycystic ovary syndrome (PCOS) resulted in 90% reduction of hair regrowth, though remained in need of regular treatments once a year owing to the underlying pathology (26). Little was gained in terms of evidence due to the lack of comparison with Control, in addition to the lack of mention for treatment protocol that could be intentional, owing to the conflicting business interest by the author. A randomized trial evaluated Intense pulse light (IPL) and long-pulsed Diode laser (LPDL) in 31 women with facial hirsutism, 19 of whom were known to have PCOS though all study subjects had to have normal testosterone levels. The study found that the median reduction in hair count was 40% for IPL and 34% for LPDL at 6 months, respectively (27). The results had no statistical significance and therefore add little information about the comparison of two devices studied, and despite its title, there was no identifiable control cohort to run alongside study groups. Lastly, the failure to isolate confounding variables such as any concurrent use of anti-androgenic medication could jeopardize the validity of data. On that note, there appears to be a lack of valid data on laser hair removal for individuals with facial hirsutism, let alone with underlying PCOS.

Adjunct approaches to laser-assisted hair removal

Eflornithine, an antiprotozoal drug, is an FDA-approved prescription cream (Vaniqa®, Allergan, Irvine, CA.) licensed for facial hirsutism in adult women (28). It has been studied as an adjunct to a long-pulsed alexandrite laser in a randomized, placebo-controlled trial in which statistically significant superiority was evident in comparison with laser treatment alone (29). Clinical effect was assessed on the upper lip in women aged 18 years or older with unwanted facial hair. Whilst individuals with clinical stigmata of hyperandrogenism were excluded from the study it could be relevant to laser hair removal in PCOS related facial hirsutism, because of the need of a higher treatment efficacy. This single-center study received public funding and with the follow-up at 6 months the outcomes did not mirror long-term efficacy. In addition, like many of the contemporary studies of laser hair removal, assessment was subjective. Safety of the treatments in combination was assured so any future long-term follow up of a trial of this kind with may prove worth-while.

Laser hair removal is inevitably a painful procedure. Topical anesthesia and skin surface cooling before, during, and after the procedure are the mainstay measures to reduce discomfort. Pneumatic skin flattening (PSF) is an adjunct technology that incorporates a vacuum in the treatment window, to generate suction on skin and stimulate pressure receptors in order to block painful input (30). This is in accordance to the gate control theory of pain. Long-term follow up of a prospective, self-controlled study demonstrated effectiveness of long-pulsed diode laser treatments, with the added advantages of the use of lower fluences, and thus less risk of adverse effects. The need of topical anesthesia was eliminated in this study (31).

A summary

Long-term follow up data is lacking, amidst little interest by the government in funding large, randomized control trials for what is otherwise regarded as cosmetic procedures. Adverse effects are few, in the most widely accepted device settings and treatment protocols. Darker skin phototypes are associated with higher rates of adverse effects owing to the additional absorption of energy by epidermal melanin. Polycystic ovarian syndrome (PCOS) is a complex endocrine disorder of androgen excess that can be defined clinically, by serology, or both. The mean reduction in hair density following multiple sessions of laser treatments is in average one third of that for individuals without the disorder. To date there is no valid efficacy data on laser hair removal for individuals with PCOS related facial hirsutism.

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