STUDY

Comparison of Long-Pulsed Alexandrite and Nd:YAG Lasers, Individually and in Combination, for Leg Hair Reduction

An Assessor-Blinded, Randomized Trial With 18 Months of Follow-up

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Objective: To compare the long-term effectiveness and safety of long-pulsed Nd:YAG and alexandrite lasers, individually and in combination, in long-term leg hair reduction.

Design: Randomized, single-center, within-participant, investigator-blinded, active-controlled clinical trial.

Setting: Private skin laser center.

Participants: Twenty individuals aged 16 to 50 years with skin phototypes III and IV.

Interventions: The medial and lateral sides of each participant's legs were randomly assigned to receive 1 of the following laser treatments: (1) long-pulsed 1064-nm Nd:YAG laser (12-mm spot size); (2) long-pulsed 755-nm alexandrite laser (12-mm spot size); (3) long-pulsed 755-nm alexandrite laser (18-mm spot size); and (4) a combination of long-pulsed 1064-nm Nd:YAG laser and long-pulsed 755-nm alexandrite laser (treatments 1 and 2). Identified areas were treated for a total of 4 sessions at 8-week intervals.

Main Outcome Measures: Hair reduction from baseline based on hair counting with digital photography by 2 blinded assessors, 8 and 18 months after the last treatment session.

Results: Fifteen participants completed the trial. The mean (SD) hair reduction 18 months after the last treatment, as measured by the assessors from digital photographs, were 75.9% (19.0%) for the 12-mm spot size alexandrite laser, 84.3% (12.4%) for the 18-mm spot size alexandrite laser, 73.6% (11.4%) for the Nd:YAG laser, and 77.8% (15.9%) for the combination therapy (analysis of variance, $P > .05$). The incidence of adverse effects (hyperpigmentation) and pain severity were significantly greater in areas that received combination therapy ($P = .001$).

Conclusions: After 18 months of follow-up, alexandrite and Nd:YAG lasers were efficacious for leg hair removal. Combination therapy did not have any additional benefit and caused more adverse effects.

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UNWANTED HAIR THAT POtentially has profound effects on psychological well-being is an exceedingly common concern for men and women. Laser-assisted photoepilation or laser hair removal, as first reported in 1996, is accomplished through destruction of the follicular unit.[1] The ability to remove hair without damaging the surrounding skin is based on selective photothermolysis. Laser hair removal provides hair-free intervals of several weeks, which lengthen with repeated treatments, and the hair regrowth becomes sparser and finer.[1,2] During the past decade, laser hair removal has become an accepted and popular means of achieving hair reduction.[1,3,4]

Recently, devices with varying wavelengths and pulse durations gave specialists a variety of alternatives to remove hair. Any laser or light source with wavelengths of about 600 to 1100 nm is absorbed by melanin and well suited for hair removal. For the most part, laser systems for this purpose range from the 694-nm ruby laser at the short end of the spectrum to the 755-nm alexandrite laser and 800- to 810-nm diode laser in the middle of the spectrum and the 1064-nm Nd:YAG laser at the end of the spectrum. An intensive pulsed-light device uses filters to limit its use to a specific portion of the spectrum.[5] Although ruby lasers were among the first to be used for hair removal, at present other lasers are more commonly used for this purpose.[6] All Nd:

YAG, diode, alexandrite, and ruby lasers have shown different but promising results.[7] Some controversial suggestions have been made regarding a combination of different laser systems such as the alexandrite and Nd:YAG systems.[6,7] We conducted this randomized clinical trial to compare the long-term efficacy and safety of Nd:YAG, alexandrite with 12- and 18-mm spot sizes, and a combination of Nd:YAG and alexandrite lasers for leg hair removal with a self-controlled design and 18 months of follow-up.

METHODS

PARTICIPANTS

Volunteers of both sexes were included if they were 16 to 50 years of age at the time of enrollment in the trial. They were excluded if they were pregnant or nursing, had any chronic systemic disease, had photosensitivity or were using any drug that facilitates photosensitivity, or had experienced any hair removal procedure during the last month.

All of participants signed the informed consent before starting any intervention. The ethics committee of the Center for Research and Training in Skin Diseases and Leprosy approved and monitored the trial, which was conducted at the Behsima Laser Center, Tehran. The trial was conducted in accord with the ethical principles provided by the Declaration of Helsinki and also the principles of Good Clinical Practice.

INTERVENTIONS

To select the target areas for laser therapy, the middle point of the connecting lines between the lateral condyle of the femur and lateral malleolus and between the medial condyle and medial malleolus of both legs were marked with a felt-tip pen. This point was used as the center of a circle template with a diameter of 1 cm for hair counting; the same point was also used as the center for the round laser probe. Two days before laser therapy, the hairs within the radius of 1 cm around the marked areas were shaved with a razor. The hair density within the radius of 1 cm around the marked areas was calculated using a commercially available hair counting device (Visiomed AG, Bochum, Germany) and special software (Visiomed AG). Photographs were taken with a digital camera (DSC/F707; Sony Corporation, Tokyo, Japan) of the target areas with 5-megapixel resolution by 1 of the authors (M.N.K.) and then assessed by 2 of us (S.K. and M.N.K.) who were unaware of the laser schedule used in the trial. The assessors counted the hairs within the targeted area using computerized high-magnification photographs. The 4 areas (the medial and lateral parts of both legs) were exposed according to a computer-generated randomization list for a single shot of each of the following laser systems in each session:

1. A 755-nm alexandrite laser (Gentlelase; Candela Corporation, Wayland, Massachusetts) with a spot size of 18 mm, fluence of 20 J/cm^2, pulse duration of 3 milliseconds, dynamic cooling device (DCD) spray duration of 50 milliseconds, and intervals of 50 milliseconds.
2. A 755-nm alexandrite laser (Gentlelase) with a spot size of 12 mm, fluence of 40 J/cm^2, pulse duration of 3 milliseconds, DCD spray duration of 50 milliseconds, and intervals of 50 milliseconds.
3. A 1064-nm Nd:YAG laser (GentleYAG; Candela Corporation) with a spot size of 12 mm, fluence of 40 J/cm^2, pulse duration of 3 milliseconds, DCD spray duration of 50 milliseconds, and intervals of 50 milliseconds.
4. A 1064-nm Nd:YAG laser (GentleYAG) with a 12-mm spot size, fluence of 40 J/cm^2, and pulse duration of 3 milliseconds in tandem with the 755-nm alexandrite laser with a 12-mm spot size, fluence of 40 J/cm^2, and pulse duration of 3 milliseconds, both of which had DCD spray duration of 50 milliseconds and intervals of 50 milliseconds. The interval between the 2 systems was 5 to 10 minutes.

All treatments were administered to the identified treatment areas by 1 of 2 operators (S.M.D. and F.B.).

The participants' eyes were covered with suitable goggles. An ice compress was used before and after laser treatment to alleviate pain and reduce adverse effects. The laser therapy was administered to the participants in 4 sessions at 8-week intervals. The participants were observed in follow-up sessions 8 and 18 months after the last laser therapy session.

RANDOMIZATION AND BLINDING METHODS

A computer-generated randomization list was designed for this 4-arm within-participant trial. The clinician who administered the treatment was responsible for opening all opaque sealed envelopes that contained the randomization information of the participants. Two investigators (S.K. and M.N.K.) who performed the assessments (hair counting) were completely blinded to the treatment type. On the other hand, the investigators (S.M.D. and F.B.) who administered the laser treatments were not involved in the assessment or the statistical analysis. Also, because the treatments were administered in a single room and the eyes of the participants were covered, the participants were blinded to treatment allocation, except for the area that received the combination laser treatment.

END POINTS

The primary trial end point was hair reduction calculated by hair counting using digital photographs by the 2 blinded assessors, at baseline and at the follow-up sessions 8 and 18 months after the last treatment session. The hairs were counted before the laser treatment and 8 and 18 months after the last session using the commercially available device (Visiomed AG) and the digital photographs. To calculate hair reduction, the difference between the hair count in 1-cm^2 areas before the first session and after each follow-up session was divided by the hair count before the first session. The hair reduction counts by the 2 assessors for each target area were averaged to use for calculations.

Secondary end points included hair reduction based on counting with the commercially available device (Visiomed AG), a visual analog scale (VAS) score for pain, and the occurrence of adverse effects such as scarring, blistering, erythema, hyperpigmentation, hypopigmentation, or secondary infection during the follow-up visits.

In every session, the amount of pain produced by the laser treatment was expressed by the participant and recorded on the VAS with a range from 0 (no pain) to 10 (unbearable pain). The VAS pain scores for each treatment group were cumulative for all 4 therapeutic sessions (range, 0-40 points).

STATISTICAL ANALYSIS

Data were entered in a commercially available statistical software program (SPSS 13.0 for Windows; SPSS Inc, Chicago, Illinois). Continuous data were reported as means (SDs). Analysis of variance assessment was used to examine the differences between the laser treatment schedules through the entire trial, whereas Tukey tests were used to compare the systems pair by pair, with consideration of all sessions. We also performed the

χ^2 test to compare the posttreatment adverse effects. Only 2-sided probability values of less than .05 were considered statistically significant.

RESULTS

The **Figure** shows a complete profile of the trial. Five participants dropped out of the trial during the 18 months of follow-up for different reasons. Included participants had a mean (SD) age of 32.6 (6.4) years, and 11 were female (55%). Fifteen volunteers (75%) had skin type of III (burns moderately, tans gradually to light brown) and 5 of the 20 (25%) had skin type IV (ie, burns minimally, always tans well to moderately brown). All of them had black hair on their legs. None of the female participants had any symptoms or signs of endocrine dysfunction such as hirsutism, adult-onset or refractory acne, extensive androgenetic alopecia, or menstrual irregularities in the medical history or results of the physical examination.

Table 1 lists the results of the average hair density and the amount of hair reduction for each of the 4 laser protocols at baseline and at 8- and 18-month follow-up sessions. Variance analysis and Tukey tests showed no significant difference between the laser systems in general or in pairs (Table 1).

The mean (SD) total VAS pain scores given by the participants in 4 sessions of laser treatment were as follows: 23.6 (8.1) in the 18-mm spot size alexandrite laser group, 22.7 (7.3) in the 12-mm spot size alexandrite group, 14.8 (7.0) in the Nd:YAG group, and 25.2 (6.6) for the alexandrite and 16.6 (6.7) for the Nd:YAG divisions in the combination treatment group.

Regarding the VAS pain scores, analysis of variance assessment showed a significant difference between the systems ($P=.001$). The pain severity in the alexandrite laser groups was significantly greater than in Nd:YAG laser group.

The only common complication that participants had was hyperpigmentation in the laser-treated area. Although this adverse effect occurred more frequently in areas treated with the 12-mm spot size alexandrite laser with a fluence of 167.4 cal/cm^2, and with a combination of lasers, these differences were not significantly different (**Table 2**). Hyperpigmentation was temporary in most of the participants; only 4 participants in the areas that were treated with combination therapy experienced this complication until the last follow-up session ($P=.005$).

Meanwhile, bullae appeared transiently in 3 target areas of 3 different participants in the second session of laser treatment, 2 of whom were treated with the combination therapy and 1 of whom was treated with the 12-mm spot size alexandrite laser ($P>.28$).

COMMENT

Responses to laser hair removal vary considerably among patients based on skin type, ethnicity, hair color, anatomical site, and the interval between treatment times.[8] To remove any source of confounding factors, we decided to focus on the alexandrite and Nd:YAG laser systems within a single patient. In the only published systematic review, Haedersdal and Gøtzsche[9] strongly criticized the literature because long-term hair removal was not documented with any laser treatment in a randomized controlled trial. In addition, it was recommended that studies have more than 6 months of follow-up (preferably >12 months).

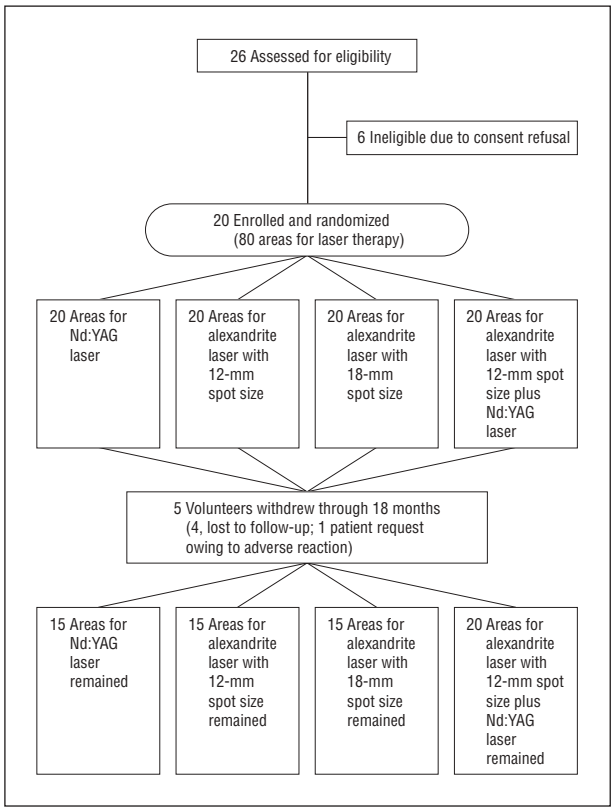

Figure. Flowchart of the clinical trial.

In our randomized, assessor-blinded trial, we found 86.0%, 79.6%, 73.6%, and 79.6% hair reduction 8 months after 4 treatment sessions with the 18- and 12-mm spot size alexandrite, 12-mm spot size Nd:YAG, and combined 12-mm spot size alexandrite and Nd:YAG lasers, respectively ($P>.26$). This reduction was maintained up to 18 months after the last treatment (Table 1), which, to our knowledge, is the longest follow-up time reported so far. This trial is, to our knowledge, the first attempt to assess the results of combining alexandrite and Nd:YAG lasers in a single session and not sequentially during several sessions. We discovered that the combination treatment will not add any more significant benefit and, unfortunately, it will cause more adverse effects.

Despite other studies showing more efficacy of the alexandrite rather than the Nd:YAG laser,[10,11] our trial results showed no significant difference between them. Rao and Goldman[12] reported a similar finding for axillary hairs. In their study, 3 sessions of 4 treatment conditions (ie, diode, Nd:YAG, and alexandrite lasers and a sequential combination of the 3 systems) were used to remove axillary hairs in 4 quadrants of both axilla. The results 3 months after the last treatment session showed that diode (mean [SD], 59.3% [9.7%]) and alexandrite (58.7% [7.7%]) lasers offer maximum hair reduction, and the combination system offered the minimum result (31.9% [10.1%]).[12] These authors attributed the lesser effect of the combination

Table 1. Average Hair Density and the Amount of Hair Reduction Measured by the Visiomed AG Device and Digital Photographs

Variable	18-mm Alexandrite Laser	12-mm Alexandrite Laser	12-mm Nd:YAG Laser	Combination Alexandrite and Nd:YAG Lasers	*P* Value[a]
		Digital Camera			
Baseline No. of hairs, mean (SD)	15.8 (4.4)	14.2 (5.9)	14.6 (6.0)	15.3 (5.5)	.86
8-mo Follow-up					
No. of hairs, mean (SD)	2.5 (2.2)	3.3 (3.6)	3.8 (2.5)	2.9 (2.4)	.58
Hair reduction, mean (SD), %	85.99 (11.62)	79.6 (19.59)	73.60 (16.6)	79.61 (18.1)	.26
18-mo Follow-up					
No. of hairs, mean (SD)	2.7 (2.4)	3.7 (3.4)	3.6 (1.6)	3.1 (1.8)	.67
Hair reduction, mean (SD), %	84.25 (12.4)	75.89 (19.0)	73.61 (11.4)	77.81 (15.9)	.25
		Visiomed AG Device			
Baseline No. of hairs, mean (SD)	14.5 (4.6)	14.7 (6.4)	14.1 (4.4)	14.(5.4)	.98
8-mo Follow-up					
No. of hairs, mean (SD)	5.6 (3.7)	5.9 (5.3)	4.8 (3.7)	5.4 (4.0)	.90
Hair reduction, mean (SD) %	61.96 (21.1)	60.12 (33.0)	60.03 (24.0)	68.05 (21.2)	.79
18-mo Follow-up					
No. of hairs, mean (SD)	6.3 (3.7)	6.2 (4.8)	5.5 (3.2)	5.0 (3.5)	.78
Hair reduction, mean (SD), %	56.99 (20.9)	56.69 (29.6)	57.33 (20.1)	65.87 (21.2)	.65

[a] Based on 1-way analysis of variance (Tukey test).

Table 2. Rate of Hyperpigmentation in Treatment Sessions and Follow-Up Visits[a]

Occurrence of Hyperpigmentation	No./Total No. of Participants (%)			
	18-mm Alexandrite Laser	12-mm Alexandrite Laser	12-mm Nd:YAG Laser	Combination Alexandrite and Nd:YAG Lasers
Before second laser session	2/17 (12)	6/17 (35)	0/17	10/17 (59)
Before third laser session	2/15 (13)	6/15 (40)	1/15 (7)	9/15 (60)
Before fourth laser session	1/15 (7)	3/15 (20)	1/15 (7)	5/20 (25)
At 8-mo follow-up	0/15	1/15 (7)	0/15	4/15 (27)
At 18-mo follow-up	0/15	0/15	0/15	4/15 (27)

[a] $P > .05$ for all comparisons.

therapy to the lesser effect of the Nd:YAG system compared with the other 2 systems. Future research is required to find better combinations of light sources.

It has been demonstrated that scattering of the laser beam is affected by the spot size.[13] One published study[14] of 3 treatments with an alexandrite laser in axilla showed a difference, although not statistically significant, of hair reduction for 18- vs 12-mm spot sizes (52% vs 42%) with the same fluence. In the present trial, we used the highest fluences for each spot size and obtained similar hair reduction, but with a higher rate of transient hyperpigmentation with the 12-mm spot size (Table 2). Generally, one may consider larger spot sizes for large areas of darker skin to use less energy. Concerning pain severity, the alexandrite laser produced more pain than the Nd:YAG system, and the difference was statistically significant ($P = .001$). Although some experts blame the alexandrite system for producing more adverse effects in darker skin,[15] in our trial the rate of burning, bullae, and hyperpigmentation showed no significant difference for each laser type, whereas only combination therapy showed a higher occurrence of the complications.

Limitations of the trial include the dropout rate of 25% and the method of assessing hair counts. Although the dropout rate is high, the effect on the results is minimized by the within-participant design. Hair counting by means of digital photographs and the commercially available device (Visiomed AG) was chosen for this trial. Although most of the published trials used digital photographs for hair assessments, we are unaware of any study comparing the reliability and validity of these 2 methods. As the baseline measurements were almost similar with both techniques, it is possible that thin hairs after laser treatment were not noticed by assessors on the digital photographs but were counted by the commercially available device (Visiomed AG), and thus the percentage of hair reduction was higher in assessments on digital photographs. In future studies, hair thickness should be measured.

The use of alexandrite or Nd:YAG laser systems alone for at least 4 treatment sessions and with 8-week intervals have long-term persistent efficacy in hair reduction with acceptable and transient adverse effects.

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