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Treatment of primary axillary hyperhidrosis with diode laser 980 nm versus Botulinum Toxin A injection

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Abstract

Background: The emotional and social sequelae of primary axillary hyperhidrosis (PAH) mandate the search for new techniques. The study aimed to compare the efficacy and safety of diode laser-980 nm versus intradermal Botulinum toxin A (BTA) in the management of PAH.
Patients and methods: This parallel-randomized controlled pilot study was conducted upon 40 PAH patients from December-2019 to June-2021 at the National Institute of Laser Enhanced Sciences (NILES), Egypt; the laser group (20 cases) and the BTA group (20 cases).
Results: The two groups were comparable regarding age, BMI, and gender (p-values > 0.05). Females constituted 60% & 65% of the laser group & the BTA group, respectively. The laser group had higher reduction of HDSS score than the BTA group at 1-month (1.40±0.50 versus 2.05±0.69; p-value = 0.002) and at 6-months (1.35±0.49 versus 2.35±0.59; p-value < 0.001). At 1-month and 6-months, the laser group had a higher reduction of the mean of moisture percentage than the BTA group (p-values < 0.001). At 1-month, there was a higher patient satisfaction in the laser group 3.5±0.61 than in the BTA group 3.10±0.71 (p-value = 0.036). At 6-months, the difference became more evident with the higher satisfaction in the laser group 3.30±0.73 than the BTA group 2.50±0.51, (p-value < 0.001). The laser group demonstrated significantly better DLQI score than the BTA group at both 1-month (p-value = 0.010) and 6-months visits (p-value < 0.001).
Conclusion: The study showed that Diode laser 980 nm is effective and safe as a treatment for PAH.
Keywords: primary axillary hyperhidrosis, Botulinum toxin A, diode 980 nm laser, quality of life.

Introduction

The abnormal excessive sweating occurring in the axillae, hyperhidrosis, is due to the hyperstimulation of the eccrine sweat glands in this area. It is caused by the cholinergic autonomic nerve fibers and is classified as primary axillary hyperhidrosis (PAH) [1]. Of course, as a common and difficult-to-manage condition, PAH has its influential emotional and social sequelae. The antiperspirants or topical aluminum chloride solutions are among the main management options. Nevertheless, they generally have provisional effects with several adverse effects such as skin rashes, itching, and burning sensations [2].

Botulinum toxin type A (BTA) is another option that had the approval by the United States Food and Drugs Administration (FDA) as a standard treatment of primary axillary hyperhidrosis by the intradermal injection [3–6]. At the level of the presynaptic cholinergic neurons, BTA effectively inhibits sweat secretion and produces paralysis at the neuromuscular (NM) junction. [7, 8]

Laser technology was once used during sympathectomy and for hair removal. Then, it has been employed for PAH [9]. Two different laser methods were used: the external laser technique and the interstitial laser technique [10].

Aiming to heat the sweat glands, the first technique, apply the laser above the skin, similar to the way used for hair removal by laser. Two studies have shown that this way is not effective and, on the converse, may even lead to heightened hyperhidrosis [11, 12]. The second technique is a derivative from that used for laser lipolysis [10, 13], where a cannula was used to introduce the fiber into the area

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under treatment. Then, the cannula is to be moved back and forth over the entire surface to be treated. Nevertheless, that may lead to adverse effects if the method is not well learned, as shown on laser liposuction[10].

Many clinical studies were conducted to investigate the efficacy and safety of this technique. Two of them conducted by Maletic and Goldman presented the most accurate data on the method used, and the outcomes obtained [14, 15]. The authors used short-pulse Nd:YAG lasers similar to those initially developed for laser liposuction in these two studies. Tumescent anesthesia is accomplished by subcutaneous (SC) infiltration with Klein's solution. The energies levels used are similar and depend on the area under treatment. The procedure took about half an hour. Then, dressings and bandages were applied for two days. [10]

By their study, Goldman A et al. (2008) aimed to present the Nd-YAG laser as an effective and safe method for PAH management. Their study included seventeen cases (15 females and two males) with PAH to be treated using a subdermal 1,064-nm Nd-YAG laser. The results were evaluated by the subjects as well as by the doctor. Minor's iodine starch test, in addition to planimetry, was used as an objective assessment. Histology also was performed on the skin after the procedure. The subdermal laser-assisted PAH management using the 1,064-nm Nd-YAG laser produced a significant clinical improvement. They observed a burn, but, was connected to a professional error. With a follow-up from 1 to about two years, the mean reduction was 72% of the Minor's test visualized area. Patients' satisfaction was achieved in 82% of them. [10, 14]

Likewise, the study's objective of Maletic D et al. (2011) was to evaluate the efficacy and safety after subdermal Nd:YAG laser treatment of PAH. It was a retrospective study conducted on thirty-two cases of patients (23 women and nine men) who underwent the subdermal 1064 nm NdYAG laser management on both of their axillae. Subjective assessment was made by the patient's self-evaluation. In addition, the objective evaluation was made using the iodine starch test. Their study showed a reduction of about 93% in the sweating area, as demonstrated by the iodine-starch test at 1-3 months after the procedure. After two years of follow-up, the subjective assessment showed that 87% of cases reported > 50% sweating reduction, 22% reported from 76 to 100% reduction. About 75% of patients declared their satisfaction with the operation and its outcomes. Also, the study reported that adverse events were transient and disappeared in three weeks. [10, 15]

According to the intensity, different laser modalities have been used, like 1064 nm Nd: YAG laser, 1440 nm Nd: YAG laser, long-pulsed 800 nm diode laser and others were used with different degrees of success in the management of PAH [14, 16-20]. However, the efficacy of laser treatments for PAH remains controversial [9].

Therefore, the rationale intended for this study was to compare the efficacy and safety of diode laser 980 nm versus intradermal Botulinum toxin A in the management of primary hyperhidrosis.

Patients and Methods

This parallel-randomized controlled study was conducted at the outpatient clinics of the National Institute of Laser Enhanced Sciences (NILES), Egypt, with 40 patients with PAH from December 2019 to June 2021. The ethical review committee approved the study. The purpose of this study was clearly explained to all patients before their enrollment.

We invited all PAH patients (male or female) who came to the NILES outpatient clinics. *For inclusion in the study*, all of the following criteria were to be fulfilled: healthy male or female between 18 - 64 years of age suffering from excessive axillary hyperhidrosis, clinically diagnosed as PAH, with

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the Hyperhidrosis Disease Severity Scale **(**HDSS**)** [21] or Malodour score [22] of three (3) or four (4), understand and accept obligation not to receive any other procedures in anatomical areas exhibiting axillary hyperhidrosis through 3 months before treatment, understand and accept the obligation and is logistically able to present for all scheduled follow-up visits.

Exclusion criteria included active bacterial or fungal infection over tested area, hydradenitis suppurativa, pregnancy or planned pregnancy or breast feeding, clinical diagnosis of secondary hyperhidrosis as excessive sweating due to hyperthyroidism and diabetes mellitus, intake of photosensitive drugs, the reception of intradermal BTA during the nine-months before the procedure, a history of autoimmune connective tissue disorders and settled skin disease in the axillae, any medical or chronic disease interferes or being contraindicated to the maneuver as significant cardiovascular disease or bleeding disorders, patients who had previous axillary laser hair reduction nor plan to have laser hair reduction while in the study, patients who had previous surgical treatment of the axillae such as axillary gland excision, liposuction, sympathectomy, or subcutaneous curettage, history of sensitivity to Lidocaine (Local Anesthesia) or Epinephrine, known allergy to BTA or contact allergy to iodine, patients on anti-platelet and anticoagulant medications, currently have implanted devices such as the cardiac pacemaker or any other internal electronic devices, and patients who refused to sign the informed consent document and/or refused to comply with all follow-up requirements.

Before randomization, all patients in both groups have laboratory assessment in the form of complete blood count (CBC), prothrombin time (PT), international normalized ratio (INR), random blood sugar (RBS), and TSH, T3 & T4.

For allocation of the participants, a computer-generated list of random numbers was used. Patients were randomized into the diode 980 nm subdermal laser group or BTA intradermal group.

Assessment

Before the procedure, room environmental temperature was ensured within 24 – 26 Celsius degrees, and skin temperature was measured using a skin infrared thermometer. Physical examination to confirm the excessive axillary sweating with a bad foul odor.

Clinical assessment was performed by the clinical scoring of hyperhidrosis (Hyperhidrosis Disease Severity Scale HDSS) and the Malodour score test to determine the degree of sweating. Scores (3) and (4) in both scorings are considered positive and suffer from excessive axillary hyperhidrosis and malodor.

Iodine starch test (before and after) the procedure, in which tincture of iodine solution and starch are applied together on both axillae. After ten to fifteen minutes, the color changed from white to blue. A positive iodine starch test indicates the presence of hyperhidrosis.

The sweating level was determined by (Digital Moisture Monitor for skin), a sweat moisture analyzer that measures the degree of moisture of the skin of axillae to ensure measuring the skin temperature all through the procedure to avoid skin injury by burning.

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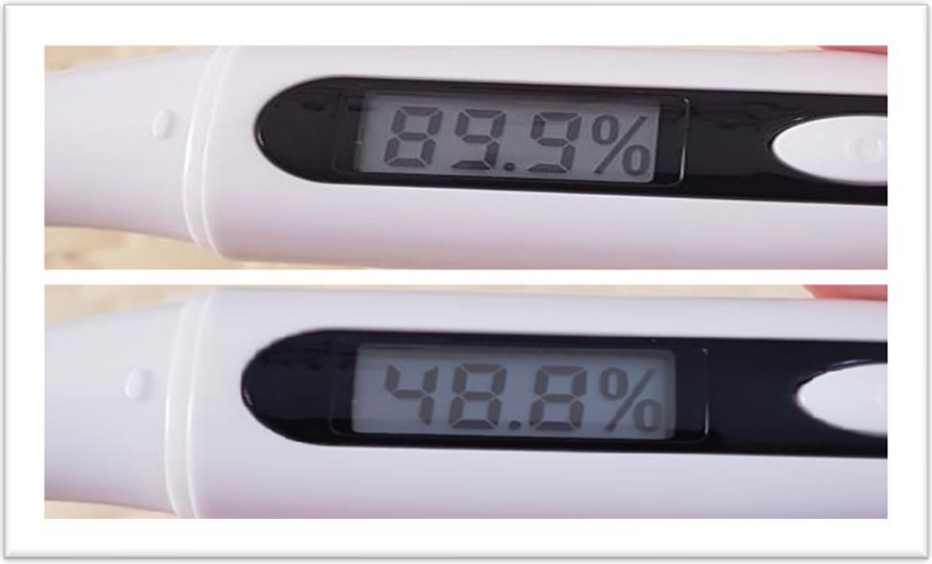

Figure 1: Moisture Monitor

Clinical assessment was also be facilitated by the use of structured questionnaires for the patient's satisfaction. These ensure consistency and objectivity of approach in the assessment and provide outcome measures that are increasingly recommended for use in clinical practice. The questionnaire responses regarding malodor and sweating were based on subjective data from the patient and their family and friends.

Procedures:

For the diode 980 nm laser group: under local anesthesia (Tumescent anesthesia), the laser is introduced subdermally to destruct sweat glands in the patient's axilla using a class 4, diode laser 980 nm (quanta system spa 21058 Solbiate Olona (VA), Italy). Power was adjusted according to the case. The time of the procedure and frequency were adjusted according to the case.

The general steps of the treatment after local anesthesia are as follows: before the operation, the underarms are coated with iodine, and the starch is used to identify the precise location of the sweat glands. Then, a 3 mm incision is made through which a cannula with an optical fiber is passed. Through this fiber-optic probe, a diode probe 0.2 mm in diameter is introduced subdermally under the skin and moved freely all arround in fanning pattern technique to cover all the desired areas in the axillary region. A diode laser beam is fired, and this beam destroys the sweat glands of the axilla.

For the BTA group, BOTOX A 100 units: injecting two units of BOTOX in every point covering the axilla.

Follow-up visits: after the procedures, all patients were followed up for six months, including assessment at one month and another at six months.

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The primary outcome measure was assessing the efficacy of both interventions via HDSS, malodor score, iodine starch test, sweating level determined by (Digital Moisture Monitor). The secondary outcomes were patient satisfaction and quality of life by the DLQI questionnaire.

Statistical analysis

A p-value of < 0.05 is considered statistically significant. SPSS software (Statistical Package for the Social Sciences, version 24.0, SSPS Inc., Chicago, IL, USA) was used. Quantitative parametric data were demonstrated as mean and standard deviation (mean ± SD). Quantitative non-parametric data were presented as the median and interquartile range (IQR). Qualitative data were presented as numbers and proportions. The Chi-square test was calculated to compare between the two groups for nominal variables and the t-test for the continuous variables. Repeated measures ANOVA tests were used for whether there are any differences between related means.

Results

There was no significant difference between the two study groups as regards to age (*p*-value = 0.979). The mean age was 37.75±12.17 and 37.85±11.70 years for the laser group & the BTA group, respectively. Also, there was no significant difference between the two study groups as regard gender (*p*-value = 0.744). Females constituted 60% & 65% of cases in the laser group & the BTA group, respectively. Also, there was no significant difference between the two study groups with regard to the BMI (p-value = 0.993). The mean BMI was 29.61±3.66 and 29.60±3.45 m^2 for the laser group & the BTA group, respectively.

Table 1: Efficacy, satisfaction and QOL in both groups

	Diode 980		**BTA**		**p-value**
HDSS	Mean	SD	Mean	SD	
Baseline	3.55	0.51	3.35	0.49	0.214
1-month	1.40	0.50	2.05	0.69	0.002
6-months	1.35	0.49	2.35	0.59	< 0.001
Malodour score					
Baseline	3.65	0.49	3.50	0.51	0.350
1-month	1.55	0.51	1.85	0.49	0.065
6-months	1.50	0.51	1.75	0.44	0.108
Moisture percentage					
Baseline	91.4%	5.6%	88.5%	5.7%	0.114
1-month	49.1%	6.3%	58.2%	5.9%	< 0.001
6-months	46.5%	6.0%	62.0%	2.8%	< 0.001
Patient's satisfaction					
1-month	3.50	0.61	3.10	0.73	0.036
6-months	3.30	0.73	2.50	0.51	< 0.001
DLQI					
1-month	23.65	1.73	22.40	1.01	0.010
6-months	23.90	2.02	17.80	1.58	< 0.001

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Hyperhidrosis Disease Severity Score

At baseline, average mean (SD) of HDSS of the laser group was 3.55 (0.51) and the BTA group was 3.35 (0.49) (p-value = 0.214).

After receiving the treatment, mean HDSS score of both groups revealed remarkably better reduction from the baseline (p-value < 0.001). Comparing between the two groups at 1 month, the laser group had significantly higher reduction of mean HDSS score than the BTA group with 1.40 (0.50) versus 2.05 (0.69), respectively (p-value = 0.002). At 6 months visit, the laser group had significantly higher reduction of mean HDSS score than the BTA group with 1.35 (0.49) versus 2.35 (0.59), respectively (p-value < 0.001).

Moisture percent

At baseline, average mean (SD) of moisture percentage in the laser group was 91.4% (5.6%) and the BTA group was 88.5 (5.7) (p-value = 0.114).

After receiving the treatment, mean of moisture percentage of both groups revealed remarkably better reduction from the baseline (p-value < 0.001). Comparing between the two groups at 1 month, the laser group had significantly higher reduction of mean of moisture percentage 49.1% (6.3%) than the BTA group 58.2% (5.9%), (p-value < 0.001). At 6 months visit, the laser group had significantly higher reduction of mean of moisture percentage 46.5% (6.0%) than the BTA group 62.0% (2.8%) (p-value < 0.001).

Malodour Score

At baseline, average mean (SD) of malodour score of the laser group was 3.65 (0.49) and the BTA group was 3.50 (0.51) (p-value = 0.350).

After receiving the treatment, mean malodour score of both groups revealed remarkably better reduction from the baseline (p-value < 0.001). Comparing between the two groups there were no statistically significant difference between groups at 1 month (p-value 0.065) and 6 months (p-value 0.108), as shown in Table 2.

Patient's satisfaction score by quartile rating scale

Comparing between the two groups at 1-month visit, there was a significant (p-value = 0.036) difference between groups with regards the patient's satisfaction. It was 3.5 (0.61) in the laser group and 3.10 (0.71) in the BTA group. However, at 6 months visit, the laser group had significantly higher satisfaction than the BTA group with 3.30 (0.73) versus 2.50 (0.51), respectively (p-value < 0.001).

Quality of life by Dermatology's Living Quality of Life Index

Comparing between the two groups at 1-month visit, there was a significant (p-value = 0.036) difference between groups with regards the patient's satisfaction. It was 3.5 (0.61) in the laser group and 3.10 (0.71) in the BTA group. However, at 6 months visit, the laser group had significantly higher satisfaction than the BTA group with 3.30 (0.73) versus 2.50 (0.51), respectively (p-value < 0.001).

The laser group demonstrated with significantly better improvement for their quality of life by DLQI score than the BTA group at both 1-month visit (p-value = 0.010) and 6-months visit (p-value < 0.001) (Figure 2).

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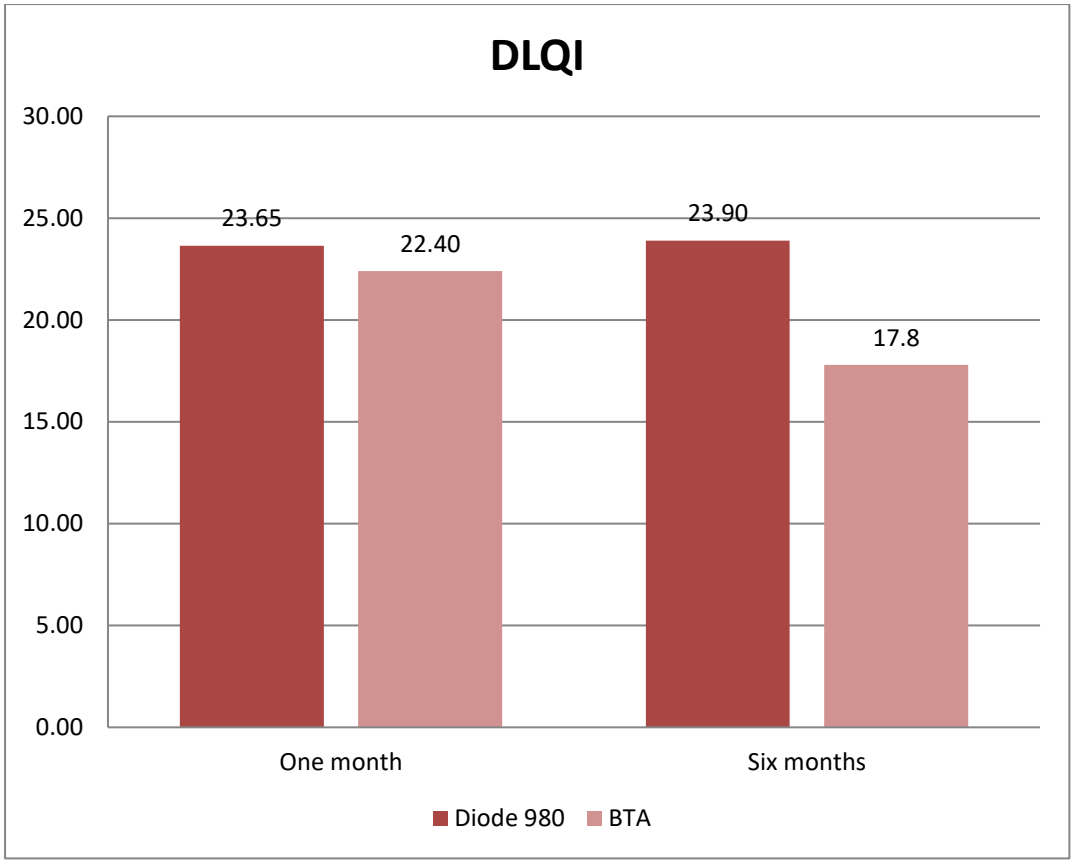

Figure 2: Quality of life by Dermatology's Living Quality of Life Index

Discussion

Primary axillary hyperhidrosis involves about 1–3% of the general population and directly affects their quality of life [23, 24]. Excessive sweating above what is biologically needed for the body to thermoregulate is referred to as hyperhidrosis. Excessive sweating can have a negative impact on a person's social life, mental health, and ability to work or study [25].

Hyperhidrosis has been linked to an increased incidence of anxiety and sadness in studies. Excessive perspiration, understandably, may be humiliating and interfere with day-to-day activities at school, work, and other social settings. Excessive sweaters are always concerned about how much they sweat and spend hours each day dealing with perspiration. [26] Hyperhidrosis has been linked to a significant reduction in health-related quality of life, particularly during the summer. Limitations in job and social connections, physical and recreational activities, and emotional and mental health issues are all examples. [27]

Our study enrolled forty patients. After receiving each treatment on both axillae, the mean HDSS score of both groups showed remarkably reduced from the baseline. By comparing between the two groups at visits (one-month and 6-months), the laser group showed a significantly better reduction of the mean HDSS score than the BTA group at both visits. Also, after receiving the treatment, the mean moisture percentage of both groups revealed remarkably better reduction from the baseline. Comparing the two

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groups at one month, the laser group had a significantly higher reduction of the mean of moisture percentage than the BTA group at the one-month visit and 6-months visit.

In addition, after receiving the treatment, the mean malodor score of both groups revealed a remarkably better reduction from the baseline. However, comparing the two groups showed no statistically significant difference between them at one month and six months. The laser group demonstrated significantly better satisfaction than the BTA group at both 1-month visit and 6-months visit. The QOL, as indicated by the DLQI, at 1-month visit and 6-months visit, the laser group showed a higher DLQI score than the BTA group.

To the best of the available literature, no direct comparison between diode laser 980 nm and BTA in the treatment of PAH could be found. A study by evidence-based review by Neumann et al. (2013), from a total of 923 patients enrolled, supported the pieces of evidence to recommend using BTA injection for the treatment of PAH [28].

A study by Heckmann et al. (2001) that conducted a randomized controlled study to compare between 200 units of BTA by comparing with the placebo and follow-up duration of 26 weeks concluded sweat production reduction by gravimetric measurement [4].

A study by Neumann et al. (2001) enrolled 320 patients with PAH to compare between 50 units of BTA with the placebo for 16 weeks follow-up time, and BTA showed significantly better sweat gland production reduction by gravimetric measurement than the placebo ($p < 0.001$). A common side effect of BTA included dry eye and dry skin [5]. However, we could not detect that effect in our study.

A study by Lowe et al. (2007) was conducted for 322 PAH patients to compare three arms comparison between 50 units of A/Ona, 75 units of A/Abo per axilla, and placebo and follow-up about 1-year duration. This study reported a percent change in at least two levels of HDSS of both botulinum toxin groups and was significantly better (75%) than the placebo with only 25% ($p < 0.001$). Botulinum toxin had a longer duration of clinical effect than the placebo [6].

The use of botulinum toxin is the most common method is to temporarily disable the sweat glands. It's quite safe, but the primary disadvantage is that the therapy isn't permanent, and the control only lasts around six months on average. The patient will require repeat injections after around six months. In the long term, it becomes quite expensive [29].

Currently, only a BTA is the only US Food and Drug Administration FDA–approved formulation for the treatment of hyperhidrosis. BTB may be useful in patients who do not respond to BTA therapy. [30]

Laser light is used to permanently destroy the axillary sweat glands by photoselectively heating sweat gland tissue without damaging any of the surrounding tissue. Some researchers found that Nd:YAG 1064 nm laser can be successfully used in axillary hyperhidrosis to cause controlled destruction of eccrine and apocrine units. [18]

However, at higher temperatures, a greater risk of superficial burns is well documented. By theory, a simultaneous emission of 924 and 974 nm wavelengths should damage both the superficial dermis and the deep cutaneous tissue. This combination could be beneficial as it allows the 924 nm to damage the sweat glands while reaching high temperatures in a lesser amount of time.In conclusion, the current study showed that Diode laser 980 nm is effective and safe as a treatment for PAH.

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Ethical approval: This study was approved by the Ethics Committee of National institute of laser in Cairo University, Cairo, Egypt.

Conflict of interest: The authors declare no competing interests.

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