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ORIGINAL ARTICLE

Pulsed dye laser versus long pulsed Nd:YAG laser in the treatment of angiokeratoma of Fordyce: A randomized, comparative, observer-blinded study

S. M. Ibrahim

Department of Dermatology, Faculty of Medicine, Al-Azhar University Hospital, Cairo, Egypt

Abstract

Background: Angiokeratoma of Fordyce is typically asymptomatic, blue-to-red papules with a scaly surface located on the scrotum, shaft of penis or labia majora. They can be treated with some locally destructive treatment modalities such as excision, electrocoagulation, cryotherapy and laser. *Objectives*: To compare the effects of the pulsed dye laser versus long pulsed Nd:YAG laser in the treatment of angiokeratoma of Fordyce. *Methods*: Twenty tow patients with angiokeratoma of Fordyce were included in this study. All participants received three sessions of pulsed dye laser on the selected side or part of lesional area and long pulsed Nd:YAG laser on the other side or part of lesional area. Two dermatologists independently evaluated the photographs of the baseline and two-month follow-up after last session using a grade system in which treatment response was categorized into six grades. *Results*: Both PDL and long pulsed Nd:YAG laser revealed statistically significant improvements in angiokeratoma of fordyce. Comparatively, there was a statistical difference between them (overall mean improvement with PDL, 61.8%, versus Nd:YAG, 77.63%; $p < 0.005$). *Conclusions*: Both PDL and 1064-nm Nd:YAG laser are effective and safe in the treatment of angiokeratoma of Fordyce with better response in Nd:YAG laser than pulsed dye laser.

Keywords

Angiokeratoma, Nd:YAG, PDL

History

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Introduction

Angiokeratomas are benign vascular lesions, characterized by ectasia of blood vessels in the upper third of the dermis, often accompanied by hyperkeratosis (1). Angiokeratoma of Fordyce, described by Fordyce in 1896 (2). Prevalence of angiokeratoma is unknown, as the lesions often unnoticed, due to lack of association with systemic effects. However, the proposed prevalence is thought to be from 0.6% between the ages of 16 and 20 years, to 16.6% in the 1970s. The lesions are most common in Caucasian and Japanese populations (3).

The precise incidence of angiokeratoma of Fordyce is unknown, but they are considered to be more common in men than in women of all ages. Angiokeratomas are typically asymptomatic, but they can occasionally bleed with slight trauma, 2- to 5-mm, dark red-to-black, round to oval papules. They are sometimes dome-shaped with hemorrhagic crusts.

Lesions have been reported on the tongue, labia majora, shaft of the penis, inner thigh, and lower abdomen. The scrotum is the most common site. The pathophysiology of angiokeratomas remains unknown, although it has been proposed that an increase in venous pressure may contribute to their formation (4). Histologically, they are composed of ectatic thin-walled vessels in the superficial dermis with acanthotic and hyperkeratotic epidermis (5).

Angiokeratoma by dermoscopy is characterized by large, well-demarcated, round-to-oval, and red-to-black areas, which are lacunar which histologically represent, dilated vessels. In addition, a white surrounding veil corresponds to the acanthotic and hyperkeratotic epidermis (6).

Many locally destructive methods, such as excision, electrocoagulation, cryotherapy, sclerotherapy and different types of laser may be used in the treatment of angiokeratomas (5). Several lasers have been used successfully in the treatment of angiokeratomas as potassium titanyl phosphate (KTP) 532 nm laser (7), carbon dioxide laser (8), a 578 nm copper vapor laser (9), long-pulsed Nd:YAG laser (10), diode laser and 585 nm pulsed dye laser (11).

Patients and methods

This was a single-center, randomized comparative observer-blinded study comparing a 595-nm pulsed dye laser treatment and 1064-nm long pulsed Nd:YAG laser treatment in patients with angiokeratoma of Fordyce.

Twenty-two patients with angiokeratoma of Fordyce were included in the present study, which was carried out within the period from July, 2013 to November 2014. All the patients were recruited from the Department of dermatology and venereology outpatient clinic, Faculty of medicine, Al-Azhar University. The study protocol was approved by the ethics committee and a written informed consent was signed by the patients. All patients

Correspondence: S. M. Ibrahim, Department of Dermatology, Al-Azhar University Hospital, Box 11843, Al-Darasa, Cairo, Egypt. Tel: +2 01005367431. E-mail: Drshadyaly@yahoo.com; Drshadyaly@azhar.edu.eg

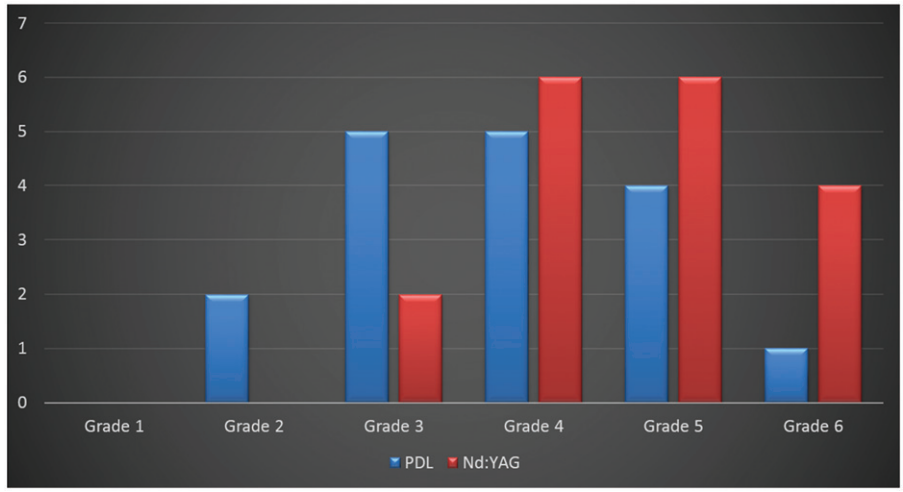

Figure 1. Comparison between PDL and Nd:YAG laser treated areas according to the six grades of improvements.

were given a detailed description of the purpose and possible outcomes of the treatment.

The patients were clinically diagnosed by the presence of the typical lesion of angiokeratoma of Fordyce. The diagnosis was based on clinical findings and dermoscopic examination. Exclusion criteria were photosensitivity, intake of photosensitive medications and history of keloid, hypertrophic scar or bleeding disorders.

Therapeutic procedures

The treatment areas were cleansed by using a mild cleanser and 70% isopropyl alcohol. A topical 2.5% lidocaine HCl and 2.5% prilocaine (EMLA; AstraZeneca AB, Sodertalje, Sweden) was applied under occlusion on the lesion. After an hour of application, the anesthetic cream was gently removed. One side or part of each subject's lesional areas was randomized to receive treatment with a 595-nm Pulsed dye laser (SynchroVasQ, Deka, Calenzano, Italy) and the other side or part received treatment with a 1064-nm long pulse Nd:YAG (Synchro Repla:y Excellium HP, Deka, Calenzano, Italy). The patients received three treatments at intervals of three weeks. All treatments were performed by a single operator.

PDL treatments were performed under the following parameters: wavelength 595 nm, spot size 5 mm^2, pulse duration 0.45 ms, and fluence 12–15 J/cm^2. Nd:YAG treatments were performed under the following parameters: wavelength 1064 nm, spot size 5 mm^2, pulse duration 20 ms and fluence 60–90 J/cm^2. The treatment was continued by using 10% overlapping pulses until an acceptable end point (transient grayness or blanching of the angiokeratoma papules).

The treated areas were cooled using ice packs immediately after the treatment. The patients were instructed to use a topical antibiotic cream twice daily for five days after each treatment.

Efficacy and safety assessments

To evaluate treatment outcome, photographs were taken using a digital camera (Canon 14 megapixel resolution, Tokyo, Japan) before treatment, one month after each session and two months after last treatment session. Two dermatologists independently evaluated the photographs using a grade system in which treatment response was categorized into six grades: Grade 1, no change after laser treatment; Grade 2, mild improvement (1–25% clearing); Grade 3, some improvement (26–50% clearing); Grade 4, moderate improvement (51–75% clearing); Grade 5, significant improvement (76–99% clearing); and Grade 6, complete improvement (100% clearing). Side effects and complications of the treatment were noted.

Data analysis

The statistical analysis was performed using SPSS, version 16 (SPSS Inc., Chicago, IL). Results were expressed as simple percentage accompanied by qualitative description of comments. The significance of differences between the data of the studied groups and the mean and standard deviation values were calculated using *t* test. *p*-Value of 0.05 or less was considered significant.

Results

Eighteen subjects from total 22 patients completed all laser treatments (three sessions) and follow-up visits. Four did not complete all treatment sessions for unknown causes. There were 16 male and two female patients, mean age 31.4 ± 5.6 (range 19–42). The lesions were located on the scrotum in eleven patients, glans penis in three, labia majora in two and penile shaft in two. The mean of disease duration was 5.05 years (range 1–10 years) (Table 1). Lesions ranged from 1 to 5 mm in diameter and varied in color from dark reddish purple to blue and in number from a few to several lesions.

Comparisons between baseline and two months after the final treatment session by two independent dermatologists revealed clinically significant improvements in all treated areas by pulsed dye laser ($61.80\% \pm 22.79$ SD) and treated areas by Nd:YAG laser ($77.63\% \pm 18.11$ SD) where outcome was complete improvement (grade 6) in four patients on the side treated by long pulsed Nd:YAG laser and one patient only showed complete improvement on the side treated with PDL. There was a significant difference between both laser treatment with superior response with long pulsed Nd:YAG laser compared to Pulsed dye laser (p value < 0.05) (Table 2), which was evaluated clinically by two dermatologists according six grades of improvement (Figure 1). Photographs of representative cases with comparative response are shown in Figures 2–4.

There was no worsening of lesions or permanent side effects in any patient just swelling, crustation in some patients, hypopigmentation and bleeding during treatment occurred in some patients especially with Nd:YAG laser. Pain score was noticed significantly higher with long pulsed Nd:YAG laser than PDL ($p < 0.05$).

Table 1. Subject demographic data and blinded investigators' evaluations.

Patient number	Age	Sex	Skin type	Duration	Location of the lesion	Improvement					
						Evaluator 2	Evaluator 1	Overall evaluation	Evaluator 2	Evaluator 1	Overall evaluation
1	26	M	IV	3	Glans penis	70	80	75	75	70	72.5
2	19	F	II	4	Labia majora	85	90	87.5	100	100	100
3	33	M	IV	5	Scrotal	75	85	80	85	80	82.5
4	35	M	V	6	Glans penis	40	40	40	75	85	80
5	26	M	III	2	Scrotal	45	50	47.5	55	50	52.5
6	29	M	III	4	Scrotal	50	45	47.5	55	50	52.5
7	30	M	IV	6	Scrotal	50	50	50	70	70	70
8	38	M	IV	7	Scrotal	100	100	100	100	100	100
9	31	M	IV	5	Penile shaft	80	85	82.5	90	90	90
10	42	M	II	10	Scrotal	15	25	20	45	45	45
11	36	M	V	7	Scrotal	50	60	55	80	90	85
12	30	F	III	4	Labia majora	50	60	55	70	75	72.5
13	28	M	III	3	Scrotal	50	50	50	70	60	65
14	33	M	IV	2	Penile shaft	90	90	90	100	100	100
15	31	M	IV	5	Glans penis	55	60	57.5	100	100	100
16	35	M	III	8	Scrotal	75	75	75	90	80	85
17	25	M	IV	1	Scrotal	20	25	22.5	50	40	45
18	39	M	IV	9	Scrotal	80	75	77.5	90	85	87.5

Table 2. Blinded overall investigators' evaluations of treatment according of six grades of improvement.

	Laser	Response						*p* Value
		Grade 1 [a]N (%)	Grade 2 *N* (%)	Grade 3 *N* (%)	Grade 4 *N* (%)	Grade 5 *N* (%)	Grade 6 *N* (%)	
Blinded investigators evaluations	PDL	0 (0%)	2 (11.11%)	3 (16.66%)	5 (44.4%)	7 (27.77%)	1 (5.55%)	<0.05*
	Nd:YAG	0 (0%)	0 (0%)	2 (11.11%)	3 (16.66%)	9 (50%)	4 (22.22%)	

[a]*N* shows number of patients that classified according to six grades of improvement.
**p* Value <0.05 is significant.

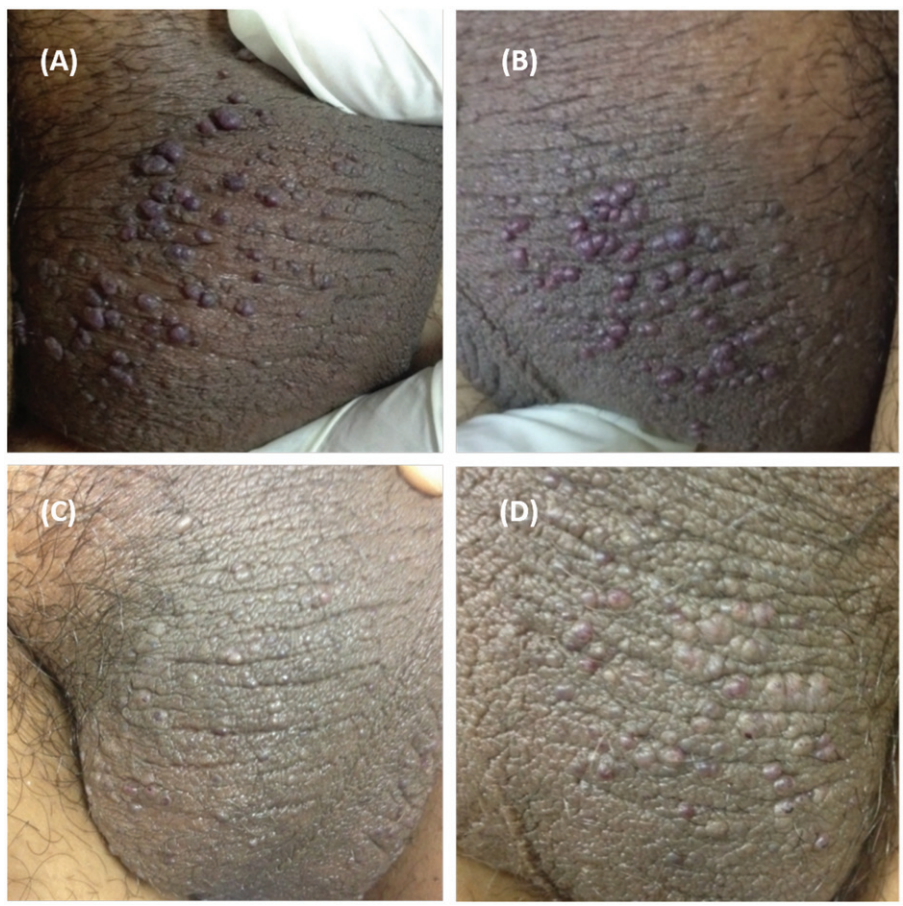

Figure 2. (A), (B) Scrotal angiokeratoma of Fordyce before the treatment. (C), (D) Significant improvement (grade 5 of improvement) after Nd:YAG laser and PDL treatments, respectively.

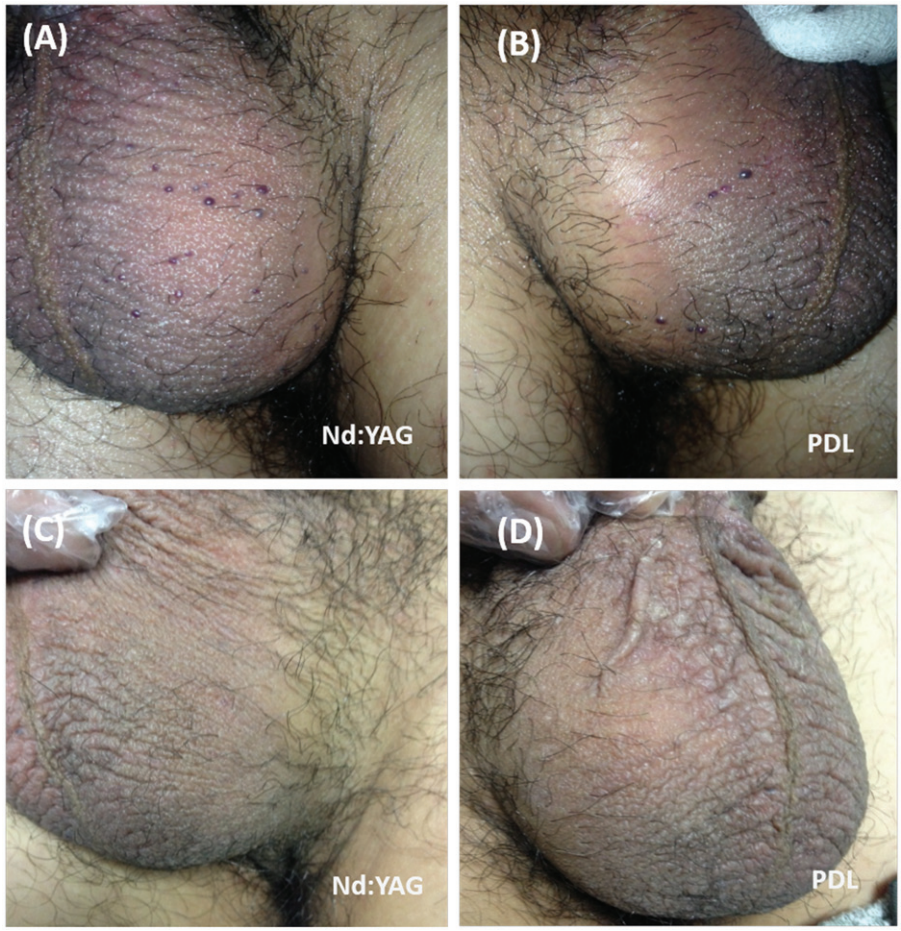

Figure 3. (A), (B) Scrotal angiokeratoma of Fordyce before the treatment. (C), (D) complete clearance (grade 6 of improvement) of the lesions after Nd:YAG laser and PDL treatments, respectively.

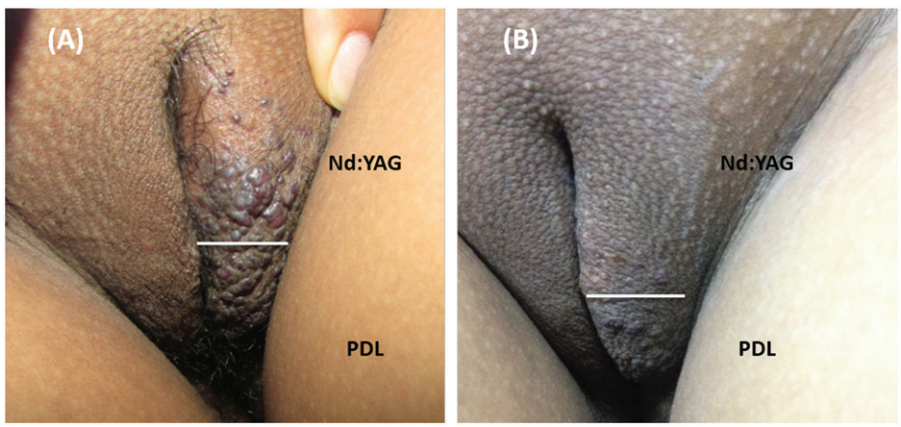

Figure 4. (A) Angiokeratoma of Fordyce on labia majora before the treatment. (B) Grade 5 improvement in area treated with PDL and grade 6 improvement in area treated with Nd:YAG laser.

Discussion

Agiokeratomas are benign vascular lesions that are typically asymptomatic. These lesions are 2–5 mm, dark red to bluish-black papules with a hyperkeratotic scaly surface. Patients ask for treatment as a result of cosmetic concerns. Angiokeratomas present a treatment challenge when they exist in large numbers. They can be treated with surgery or locally destructive treatment modalities such as electrocoagulation, cryotherapy and various laser systems (12).

Several lasers have been used successfully in the treatment of angiokeratomas such as 578-nm copper laser, argon laser, 532-nm KTP laser, pulsed dye laser and long pulsed Nd:YAG laser (13). In addition, ablative lasers such as erbium-doped yttrium aluminium garnet lasers have been used to remove the hyperkeratotic epidermis before treatment with a vascular laser (14).They have reported good permanent cosmetic results with minimal adverse effects.

In the present study, the rationale was to compare the effect of PDL versus the effect of long pulsed Nd:YAG laser, observing the effect on angiokeratoma of Fordyce lesions. To our knowledge this is the first randomized, comparative, split trial to evaluate the efficacy and adverse effects of the 595-nm PDL and 1064-nm long pulsed Nd:YAG lasers in the treatment of angiokeratoma of Fordyce.

In this study, all of the patients revealed a significant improvement in number of angiokeratoma of Fordyce lesions on both sides of treatment with no significant side effects.

The difference in improvement between both sides was significant ($P < 0.005$). In our patients, we observed a higher clearance rate with long pulsed Nd:YAG laser in comparison to pulsed dye laser treatment so the long pulsed Nd:YAG laser was more effective than PDL in the treatment of angiokeratoma of Fordyce.

Several studies have reported significant effect of PDL on the angiokeratoma of Fordyce with variable percentage. Lapidoth and colleagues demonstrated the efficacy of 585-nm PDL in the treatment of angiokeratomas of Fordyce. After two to six treatment sessions, all 12 patients' demonstrated improvement, seven had 75–100% clearance, and five had 50–75% response. Their approach was based on the higher safety profile of the PDL compared to the Nd:YAG laser, which is associated with more scarring and greater pain (11).

However, successful treatment of angiokeratomas using a 1064-nm Nd:YAG laser has also been described. Civas and colleagues successfully treated two patients using a 1064-nm Nd:YAG laser, with complete clearance after two treatment sessions (12). In another study, Ozdemir and colleagues used a 1064-nm Nd:YAG laser to treat angiokeratomas of Fordyce in 10 patients, with significant improvement seen in six patients, moderate improvement in two patients and complete improvement was achieved in one patient after six treatment sessions (13).

The long pulse Nd:YAG laser treated side has shown a significant improvement than the PDL treated side in angiokeratoma of Fordyce lesions, which could be explained by the fact that Nd:YAG laser has a longer wavelength and greater penetration depth than PDL on hyperkeratotic lesions which could cause the complete destruction of angiokeratoma of Fordyce.

These authors speculated that the greater depth of penetration achieved using the Nd:YAG laser provides benefit over PDL when treating significantly hyperkeratotic lesions. Sommer and colleagues reported improvement of extensive angiokeratoma of Mibelli using a 1064-nm Nd:YAG laser, although their patients developed persistent atrophic scarring and hyperpigmentation (10).

However, partial response has been achieved in some patients with this laser because large lesions of angiokeratomas accompanied with hyerkeratosis may need to be wavelength characterized by more penetration depth to get the effect. Because skin penetration depths of long-pulse Nd:YAG laser are high, it provides an advantage over the pulsed-dye laser.

Conclusion

Both treatments either the PDL or Nd:YAG laser are effective and safe therapeutic option in the treatment of angiokeratoma of Fordyce with better response in Nd:YAG laser than pulsed dye laser.

Declaration of interest

I have no conflict of interest to declare, sources of support and disclosure of funding received for this work from any of the organizations.

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