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CLINICAL REPORT

Variable Pulse Frequency-doubled Nd:YAG Laser Versus Flashlamp-pumped Pulsed Dye Laser in the Treatment of Port Wine Stains

SUSANNE LORENZ, KATHRIN SCHERER, MONIKA BEATRIX WIMMERSHOFF, MICHAEL LANDTHALER and ULRICH HOHENLEUTNER

Department of Dermatology, University of Regensburg, Germany

The flashlamp-pumped pulsed dye laser (FPDL) is regarded as the gold standard in the treatment of port wine stains. The purpose of this prospective, intra-individual, comparative clinical study was to investigate whether a frequency-doubled variable pulsed Nd:YAG laser (frequency-doubled Nd:YAG) is equally as safe and effective as established lasers. Forty-three patients with port wine stains were included in the study. Test treatments were performed using the frequency-doubled Nd:YAG laser (532 nm; 4 mm Ø; 5–50 ms; 5.5 to 15 J/cm^2) versus the FPDL (585 nm; 450 μs; 7 mm Ø; 6 J/cm^2). After 6 weeks, a full lesional treatment was performed using the device and the parameters showing the best clearance and the fewest side effects. The clearance of the lesions was generally good to fair. With the exception of poor results at 5 ms and 5.5 J/cm^2 with the frequency-doubled Nd:YAG laser, there were no significant differences between the two laser devices. Scar formation, nevertheless, occurred in only 3% of the FPDL-treated sites versus up to 18% of the frequency-doubled Nd:YAG sites, increasing with pulse duration. In port wine stains, the FPDL remains the therapy of choice because of the somewhat better results and a lower frequency of side effects, especially scarring. *Key words: clearance; FPDL; PWS; scarring; side effects.*

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Susanne Lorenz, Department of Dermatology, University of Regensburg, DE-93053 Regensburg, Germany. E-mail: Lorenz@rkdernw1.ngate.uni-regensburg.de

The flashlamp-pumped pulsed dye laser (FPDL) is regarded as the gold standard in the treatment of port wine stains (PWS), especially in the treatment of children (1–4). Although permanent side effects, e.g. scar formation, are rare (5), transient side effects such as blue to black maculae, crusting and hypo- or hyperpigmentation are common (4, 5). The wavelength at 585 nm is a compromise between blood absorption and penetration depth (6–8). According to van Gemert et al. (6) and Dierickx et al. (9) a pulse duration between 1 and 10 ms is regarded as the optimum for the treatment of PWS vessels (up to 200 μm) following the theory of selective photothermolysis (7).

Some time ago, a frequency-doubled Nd:YAG laser became available (10, 11) with interesting irradiation parameters (2–50 ms at 4 mm spot size, fluences up to 38 J/cm^2) for the treatment of vascular lesions. The wavelength of 532 nm shows a good HbO_2-absorption with slightly higher melanin absorption than at 585 nm or 595 nm. Theoretically, the long pulse duration should make it possible to treat vessels larger than 200 μm in diameter. Owing to longer pulse duration and higher melanin absorption, a cooling device is required which is integrated into the laser handpiece to reduce epidermal damage.

Our aim was to evaluate the efficacy and safety of the frequency-doubled Nd:YAG laser in the treatment of PWS in an intra-individual comparison with the FPDL which is established for this indication.

PATIENTS AND METHODS

Patients

Forty-three patients (12 males and 31 females; age range 2–59 years, mean 24 years (males 19 years, 10 months; females 25 years, 9 months)) were included in the study after they had given their informed written consent. All patients had Fitzpatrick skin types I to III. The PWS colors included light pink ($n=2$), pink ($n=6$), red ($n=22$), dark red ($n=7$) and purple ($n=6$). Lesions showed a typical distribution of 59% ($n=28$) in the head and neck region, 10% ($n=5$) in the trunk and 31% ($n=10$) in the extremities.

Laser devices and treatment parameters

A frequency-doubled Nd:YAG laser (532 nm; Versa Pulse C (Vegas); Coherent Inc., Santa Clara, CA) with 4 mm spot size and the following pulse length/fluence combinations was used: 5 ms/5.5 J/cm^2, 10 ms/9.5 J/cm^2, 15 ms/12 J/cm^2, 20 ms/15 J/cm^2, 30 ms/15 J/cm^2, 40 ms/15 J/cm^2, 50 ms/15 J/cm^2. At 5 to 15 ms, the fluence used represented the maximum fluence possible with this device at 4 mm spot size. In areas treated with 20 to 50 ms pulses we chose the fluences as proposed by the distributor of the laser device. All treatment areas were precooled with ice cubes for 5 to 10 s. Treatment was carried out using the integrated "chilled-tip" handpiece at 4°C (VersaSpot Chilled Tip; Coherent Inc.), and a post-treatment cooling with a "cold-pack" was applied for 15 min.

As the standard laser, we used the FPDL (585 nm; SPTL 1B; Candela Corp., Wayland, Mass.) with 7 mm spot size, 450 μs pulse duration and a fluence of 6 J/cm^2. These

treatment parameters were our standard parameters used for test areas in the outpatient laser department. No cooling was used with this laser.

Treatment regimen

For sensitive patients and in children, we applied topical anesthesia with EMLA™ cream. No sessions were performed under general anesthesia.

Patients were treated at intervals of 6 weeks. At the first visit, each patient was given multiple test treatments with different parameters of the frequency-doubled Nd:YAG (as given above) and a single test area with the FPDL. We started with the FPDL area and then continued with the frequency-doubled Nd:YAG laser areas, beginning with 5 or 10 ms and corresponding fluences. Depending on the size of the lesion, we performed as many test areas as possible, with the aim of targeting at least 6 spots with each laser. In larger lesions, up to 20 test spots were applied. The test areas were performed in vertical rows at the same site of lesion, to prevent clearance biases. At the follow-up visits, full lesional treatments were applied using the laser parameters with the best results and fewest side effects. If FPDL and frequency-doubled Nd:YAG laser showed an identical result, the lesion was divided, and one half was treated with the FPDL device, and the other half with the frequency-doubled Nd:YAG laser (using the parameters showing the best results).

Documentation and evaluation

Photographs of all the sites were taken using the same camera and films. Treatment outcomes were evaluated by comparing the pretreatment photographs with the patient's lesions as presented at the treatment session. Results were ranked according to 5 clearance scores: 4 = excellent (75 – 100% lightening), 3 = good (50 – 75% lightening), 2 = fair (25 – 50% lightening), 1 = bad (<25% lightening), 0 = no clearance. Three doctors working in the outpatient laser department carried out all the treatments, evaluations and photography. The doctor evaluating the results was blinded to the parameters used in the former session, in so far as the evaluation took place in a semi-blind way.

Side effects were documented as hypo- and hyperpigmentation or scar formation (atrophic or hypertrophic). Therapy sequelae such as blistering, purpura or crusting were documented as reported by the patient.

Pain was evaluated during the performance of the test areas using a patient's check tag handed out to the patients (>6 years) treated without any anesthesia with the possibilities: disturbing only, light, moderate and severe pain.

For statistical analysis, MS Excel™, MS Access™ and Jandel Scientific Sigma Stat™ were used. Due to relatively small groups, each frequency-doubled Nd:YAG test site versus FPDL site was statistically tested with the Mann – Whitney rank-sum test.

RESULTS

Test areas

Comparing the FPDL- (7 mm Ø; 6 J/cm^2) treated test areas with the frequency-doubled Nd:YAG test sites, no significant differences in clearance could be seen at the pulse lengths 10, 15 and 30 – 50 ms. In the 5 ms/5.5 J/cm^2 and in the 20 ms/15 J/cm^2 test areas, the frequency-doubled Nd:YAG proved to be significantly inferior ($p = 0.003$ and $p = 0.045$) to the FPDL. The exact results, mean improvement scores and SD are presented in Table I.

Half of the PWS that responded more favorably to the frequency-doubled Nd:YAG were located in the facial area and half in the extremities. Colors were 3 red, 1 dark red and 2 purple. The age of those patients ranged from 13 to 52 years with the median at 37 years. The median age of all patients was 24 years.

Full lesional treatments (n = 12)

Twelve patients were given full lesional treatment. In one case the lesion had to be divided in half owing to identical results with both lasers. In full lesional treatment with the frequency-doubled Nd:YAG we achieved 1 excellent, 3 good, 2 moderate and 1 poor result. The average was good ($n = 7$; 2.6 ± 0.98). Fig. 1 shows a typical, excellent result of frequency-doubled Nd:YAG therapy in a small PWS. Furthermore, FPDL (7 mm Ø; 6 J/cm^2) -treated lesions showed an average good result ($n = 7$; 3.4 ± 0.79) with 4 excellent, 2 good and 1 moderate result. The mean clearance scores showed a trend towards a better result in FPDL-treated areas ($p = 0.128$).

As therapy sequelae, the FPDL-treated lesions showed the typical blue – black macules. The frequency-doubled Nd:YAG-treated areas showed only blanching

Table I. *Clearance rates in port-wine stain test areas*

			Clearance score (n)						
Laser	Parameter	N	4 (excellent)	3 (good)	2 (fair)	1 (bad)	0 (none)	Mean score	SD
Fd Nd:YAG	5 ms/5.5 J/cm^2	10	0	0	2	6	2	1	0.67
Fd Nd:YAG	10 ms/9.5 J/cm^2	16	3	3	4	4	2	2.1	1.34
Fd Nd:YAG	15 ms/12 J/cm^2	25	5	6	7	4	3	2.2	1.30
Fd Nd:YAG	20 ms/15 J/cm^2	13	0	3	6	2	2	1.8	1.01
Fd Nd:YAG	30 ms/15 J/cm^2	8	1	2	1	2	2	1.8	1.49
FPDL	7 mm/6 J/cm^2	25	9	6	4	4	2	2.6	1.35

Fd Nd YAG: frequency-doubled Nd YAG; FPDL: flashlamp-pumped pulsed dye laser.

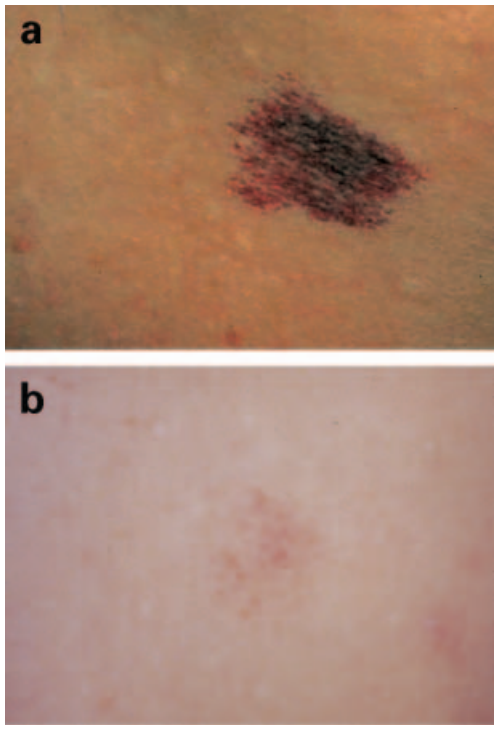

Fig. 1. Port wine stain on the décolleté of an 18-year-old woman, (*a*) before treatment, and (*b*) after one full lesional treatment with the frequency-doubled Nd:YAG laser (15 ms/12 J/cm^2).

or white to light grey spots. Crusting appeared in nearly all FPDL or frequency-doubled Nd:YAG-treated areas. The frequency of side effects after the test treatments, e.g. hypo- or hyperpigmentation and scarring, is shown in Fig. 2. While changes in pigmentation were present in approximately 20 to 30% with both laser types, post-inflammatory textural changes and scarring increased from 3% with the FPDL to 6 respectively 18% in the frequency-doubled Nd:YAG- (15 ms and 30 to 50 ms) treated areas.

The patients characterized the frequency-doubled Nd:YAG laser as causing light (33%), moderate (57%) and severe (10%) pain, the FPDL as causing light (47%), moderate (47%) and severe (6%) pain.

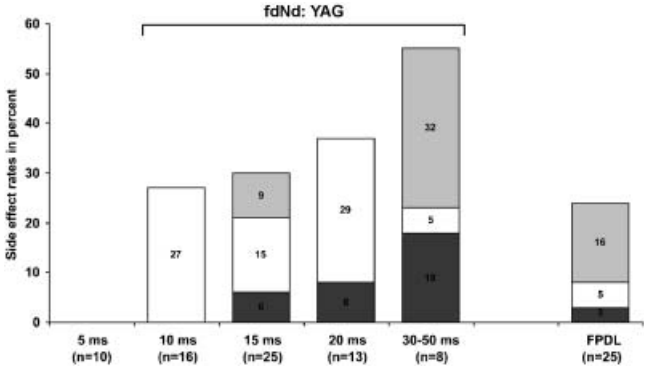

Fig. 2. Side effects and complications after the test treatments. ■Scar formation + post-inflammatory textural changes; □ hypo-pigmentation; ■ hyperpigmentation. fdND:YAG: frequency-doubled Nd:YAG laser; FPDL: flash lamp-pumped pulsed dye laser.

DISCUSSION

Since the 1980s, the treatment of PWS with the FPDL device has been regarded as the gold standard (1–3, 12, 13). Other treatment options were the Argon laser, which has a high scar formation rate especially in children (14), and the Nd:YAG laser with similar problems and the need for general anesthesia (15). These devices have therefore become obsolete, especially in the treatment of children.

Recently a Nd:YAG laser with 532 nm and a pulse duration of up to 50 ms has become available. This device can provide pulse lengths from 2 to 50 ms, which are in the range of the pulse lengths between 1 and 10 ms postulated to be ideal for PWS treatment (6–9). Like the FPDL at 585 nm, the frequency-doubled Nd:YAG laser's wavelength of 532 nm lies close to but not on a peak of the HbO_2 absorption curve, providing a greater vessel penetration depth (16). Nevertheless, compared to 585 nm, the melanin absorption of the 532 nm wavelength is higher, which leads to more energy deposition in the basal epidermal layer. Therefore, to reduce epidermal damage, cooling is required.

With respect to the clearance rates, our study proved the frequency-doubled Nd:YAG to be as effective as the FPDL in the treatment of PWS.

In the test areas, which are known to correspond well with later clearance rates of the full lesion in multiple treatments (17), the sites treated with 10 or 15 ms pulse duration showed similar results to those with the FPDL.

Those sites that responded better to the frequency-doubled Nd:YAG seemed to be darker (red to purple) than the average site and the patients seemed to be older (median age 37 years). Although the number of patients is small, this fits with the theory that in older patients and in darker PWS, where the vessels are more ectatic and deeper in the dermis, a longer pulse duration and a wavelength with lower absorption in hemoglobin will lead to better results.

In full lesional treatment, the clearance rates of frequency-doubled Nd:YAG and FPDL were almost equal but showing a non-significant trend in favor of the FPDL. However, owing to the low number of fully treated areas, and because only one therapy was performed, these results are only preliminary and will have to be confirmed in larger patient groups.

In the test areas, pulse durations >15 ms were not as effective as those up to 15 ms. This concurs with the theory of selective photothermolysis, which predicts a loss of selectivity and an increased heating effect of the surrounding dermis when a vessel is treated with a pulse duration longer than its thermal relaxation time, which is calculated to be 0.1–10 ms for PWS vessels with a diameter between 10 μm and 180 μm (18).

Since the clinical results with the frequency-doubled Nd:YAG and the FPDL seem comparable, any differences in the side effects and complications of

the two laser devices become especially important. According to the patients, the pain during treatment was almost equal to that with the FPDL and the frequency-doubled Nd:YAG, with the frequency-doubled Nd:YAG seeming to be a slightly more painful. The blue–black discoloration after FPDL treatment (4), however, is not present with frequency-doubled Nd:YAG treatment, which makes the post-treatment period more acceptable for the patient. The pigmentary changes after FPDL treatment observed in our study were comparable to those reported in the literature (4, 5, 19, 20). In the frequency-doubled Nd:YAG-treated lesions, the rate of pigmentary changes increased from 0% at 5 ms pulse duration to 37% at a pulse duration of 30 ms and longer. The higher melanin absorption of the frequency-doubled Nd:YAG and the unspecific heat deposition with the long pulse duration are probably responsible for this (21). Since pigmentary changes, even if disturbing, are usually reversible (20), scar formation as an irreversible complication is the more important side effect.

With FPDL treatment, our study results concur well with a previous report of (3.4 to 5%) scar formation, with a moderate increase from small test areas to repeated full lesional treatments (11). In the frequency-doubled Nd:YAG areas, scarring rates of 6% (15 ms) up to 18% (30 ms and longer) showed a clear correlation to the pulse duration. An association between an increase in scar formation and the extent of the area treated could also be seen.

Taking clearance rates, pain and side effects into account, the frequency-doubled Nd:YAG seems to be comparable to the FPDL for the treatment of PWS only for pulse durations shorter than 15 ms. At longer pulse lengths, the increasing rate of thermal side effects limits its use, like that of the argon laser, to dark or hypertrophic PWS in adults.

An improvement in clearance rates and perhaps even better results than with FPDL treatment might be obtained if higher fluences at 5 or 10 ms and spot sizes $\geq$4 mm were available. Technical improvement of the frequency-doubled Nd:YAG laser leading to higher pulse energy in the pulse lengths of 5 or 10 ms and to larger spot sizes would certainly be of interest in the treatment of PWS and other vascular lesions.

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