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ORIGINAL ARTICLE

Does dye laser treatment with higher fluences in combination with cold air cooling improve the results of port-wine stains?

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Abstract

Background and objective The use of cold air cooling (CAC) and cryogen spray cooling during dye laser treatment of port-wine stains (PWS) has become a standard in recent years. Still unsolved is the question of which fluences are necessary in combination with CAC in order to achieve an optimum clearance and the lowest possible rate of side-effects.

Study design In a prospective study, we treated 11 patients with PWS with pulsed dye laser (Photogenica V®, Cynosure, λ = 585 nm, ι_p = 0.5 ms, spot size = 7 mm). Each PWS was partitioned into three areas: (area 1) 6 J/cm^2 without CAC, (area 2) 6 J/cm^2 with CAC (level 4), (area 3) 9 J/cm^2 with CAC (level 4).

Results Area 3 (mean, 59%) showed a slightly better clearance than area 1 (mean, 57%); in area 2, we observed a reduced clearance (mean, 45%). Compared with area 1, we achieved a reduction of pain through CAC in areas 2 and 3. The healing periods as well as the rate of side-effects were comparable in all areas.

Conclusion We observed a slight but not statistically relevant increase in clearance with the use of higher fluences and CAC compared with lower fluences without CAC. Because pain is lowered significantly when using CAC, and because this makes the treatment more comfortable for the patients, we tend to recommend the use of higher fluences (9 J/cm^2) with simultaneous CAC for treating PWS.

Introduction

The treatment with pulsed dye laser has been an accepted standard method for the treatment of port-wine stains (PWS) for 15 years now. The clearance rate depends mainly on the laser fluence and on the age, localization, colour, depth, and diameter of the vessels.[1–8] After an average of four to eight treatment sessions, only about 40% of patients had achieved a 75% lightening of their PWS.[4,9,10] Therefore, studies with different wavelengths, pulse lengths, and fluences were carried out in the past years in order to optimize dye laser therapy especially for those patients.[11–19] Chang and Nelson as well as Chiu *et al*. recently reported about an improved clearance of PWS through the application of higher fluences and simultaneous use of cryogen spray cooling (CSC).[20,21]

It was the objective of our study to evaluate the effects of higher fluences (9 J/cm^2) in combination with cold air cooling (CAC), and the effects of 6 J/cm^2 with and without cooling, particularly regarding clearance and the rate of side-effects.

Materials and methods

Between July 2004 and January 2005, we carried out a randomized prospective study with a total of 11 patients (10 females and 1 male), all of whom had congenital PWS. All patients had voluntarily agreed to participate in the study. The PWS had been untreated with 10 patients and pretreated with the argon laser with one patient.

The age of the patients ranged from 5 to 56 years, with a median of 30 years. For safety reasons, we accepted only

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Table 1 Side-effects

		With cooling	
Side-effects	**Without cooling (6 J/cm²)**	**6 J/cm²**	**9 J/cm²**
Purpura/crusting	Healing period ∅ 11 days	Healing period ∅ 10 days	Healing period ∅ 12 days
Blisters	None	None	None
Hypopigmentation	1 patient	1 patient	1 patient
Scarring	None	None	None

Table 2 Degree of pain (1, no pain to 10, very strong pain)

	Pain from 1 to 10		
Patient	**6.0 J/cm² without cooling**	**6.0 J/cm² with cooling**	**9.0 J/cm² with cooling**
1	8	5	6
2	7	4	5
3	5	8	7
4	10	6	5
5	5	3	2
6	4	3	3
7	6	5	7
8	6	2	6
9	5	2	4
10	8	3	6
11	9	6	7
Average:	6.6	4.3	5.3

patients with Fitzpatrick[22] skin types I to III. The sizes of the PWS ranged from 13 to 3600 cm^2.

Two of the PWS were pink, six were red, and three were purple. They were located on the cheek, neck, back, and legs.

The treatment was done in one session with pulsed dye laser (Photogenica V®, Cynosure, Chelmsfort, CA; $\lambda = 585$ nm, $\iota_p = 0.5$ ms) and a spot size of 7 mm. Small PWS were partitioned into three areas; with bigger ones, we selected an area of 10 × 10 cm and partitioned it into three areas: (area 1) 6 J/cm^2 without cooling, (area 2) 6 J/cm^2 with cooling, (area 3) 9 J/cm^2 with cooling. For CAC, we used the device Cryo® 5 (Zimmer-Elektromedizin, Ulm, Germany) with cooling level 4. This cooling device generates from ambient air a continuous stream of air of 500 to 1000 L/min and a possible minimum temperature of –30 °C. Given an initial temperature of 32 °C, this temperature yields a skin temperature of 15 °C within 8 s.[17]

The side-effects were assessed by the treating doctors and the patients themselves after 10 min, 3 days, and 6 weeks. The extent of pain was evaluated with a numerical scale (1, slight; 10, strong pain), other side-effects (purpura, blisters, crusting, hypopigmentation, and hyperpigmentation) by healing time in days.

After 6 weeks, clearance was evaluated by the patients themselves and by four independent medical doctors (0%, 10%, 20%, ... 100%). Photos were taken before and 6 weeks after treatment with a Canon EOS100 camera and an Agfa Ctx100 film.

Results

Side-effects like crusting, purpura and, in one case, hypopigmentations, occurred in all areas.

Slight crusting occurred without cooling in four cases and with cooling in two cases. With one patient, hypopigmentations were observed in all three areas. Blisters or scar formation did not occur at all.

The average healing times were 11 days in area 1, 10 days in area 2, and 12 days in area 3 (Table 1).

Compared with area 1, we achieved a considerable reduction of pain in areas 2 and 3 by using CAC (Table 2). Regarding the extent of pain, area 1 showed an average value of 6.6, area 2 showed 4.3, and area 3 showed 5.3. According to a Wilcoxon signed rank statistical test, treatment in area 2 was significantly less painful than in area 1 at $P = 0.05$.

A comparison of areas 1 and 2 shows that clearance in area 2 is lower with five patients (on average from 64%

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Table 3 Average clearance and localization of PWS

Patient	Localization	Clearance in percentage		
		6.0 J/cm² without cooling	6.0 J/cm² with cooling	9.0 J/cm² with cooling
1	Back	90	50	90
2	Cheek	80	50	80
3	Cheek	30	20	30
4	Cheek	30	10	40
5	Neck	90	40	90
6	Lumbar	100	100	100
7	Sacral	90	90	90
8	Neck	70	70	90
9	Leg	0	0	0
10	Neck	10	10	20
11	Leg	40	60	20
Average clearance in percentage		57	45	59

fig. 1 (a) Before therapy. (b) Ten minutes after therapy (left area, 6 J/cm² without cooling; centre area, 6 J/cm² with cooling; right area, 9 J/cm² without cooling). (c) Six weeks after therapy.

to 34%, Table 3), the same with five patients (average clearance 54%) and higher with one patient (from 40% to 60%).

A comparison of areas 1 and 3 shows higher clearance for area 3 in three cases (on average by 13%), lower clearance (by 20%) in one case, and no change in seven cases (average clearance of 69%).

When comparing areas 2 and 3, we observed higher clearance for area 3 in seven cases, no difference in three cases, and lower clearance in area 3 in one case.

On average, we had the best clearance rate in area 3, directly followed by area 1, and the worst clearance in area 2 (area 1, 57%; area 2, 45%; area 3, 59%; fig. 1a–c).

It seemed that clearance was dependent on the colour of the PWS. Red PWS showed the best (68–73%), pink ones medium (30–85%), and purple ones the worst clearance rates (13–20%).

Discussion

The treatment with the 585-nm pulsed dye laser has been an accepted standard therapy of PWS for many years; it is based on the effects of selective photothermolysis and thermal relaxation time.[23] Accompanying cooling methods (cryogen spray and cold air) have also become part of the standard therapy; they help to reduce pain and side-effects.[1,12,14–17,20,24–29]

In many cases, there is still an incomplete or unsatisfactory lightening of PWS. Thus, it is necessary to conduct more studies to evaluate the use of different parameters; the most suitable method is the direct side-by-side comparison. Another open question is the safety and efficacy of higher fluences in combination with the use of CAC.

In a retrospective study, Chang and Nelson evaluated a total of 196 patients with PWS; each PWS was treated with only one set of parameters (8–10 J/cm², 0.5 ms, 7 mm, with CSC or 5–7 J/cm², 0.5 ms, 7 mm, without cooling).[20] Significant improvement of clearance due to fluence increase was observed only in those PWS that had severity score 2 (well-defined borders, uniform lesion with no areas of normal skin, plus raised or thickened lesion, plus modularity or hypertrophy of involved anatomic structure). The question of why patients with PWS with severity score 1 (faint, barely discernible

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borders plus well-defined borders with areas of normal skin interspersed within the lesion) did not profit from the increased fluence is not discussed in the paper. At the same time, there was no increase in the rate of side-effects, which is why they principally recommend to use CSC with higher fluences.

Chiu *et al.*, too, evaluated in a prospective study whether higher fluences can augment PWS clearance rates.[21] To this aim, they treated each PWS with two different sets of parameters (585 nm, 7 mm, 1.5 ms, average fluence 10.7 J/cm^2 plus CSC and 585 nm, 7 mm, 1.5 ms, average fluence 6.5 J/cm^2, no cooling). They found that PDL-CSC was more effective than PDL alone for blanching of PWS in Chinese patients. Moreover, PDL-CSC was better tolerated and resulted in a lower incidence of acute adverse effects such as blistering.

In our study, we observed a slight but not statistically relevant increase of clearance by using higher fluences and CAC compared with lower fluences without CAC. We think that the following reasons may explain this.

First, the vascular architecture changes, even in the same lesion. Optimal treatment settings are predicated on vessel diameter and vessel depth.

Second, CAC is a bulk mechanism for cooling. Thus, it is likely that, when cooling the vessels to be treated and the surrounding tissue, we do two things to them: (i) we make them smaller targets, because vessels contract when cooled. This mainly affects the deeper vessels that have autonomic innervation and 'feed' the PWS. Their contraction decreases the perfusion in the PWS and thus the target vessel size. Due to an absolute or relative deficiency in autonomic innervation of the PWS post-capillary venules in the papillary plexus, these vessels do not react to temperature changes; (ii) we make them colder, thus increasing the amount of heating required to heat them to a damage temperature. Both of these work against successful treatment because higher fluences are required in order to reach efficacy. This can be discounted to a certain extent because the purpura lasted about as long under all conditions, which suggests that the energy was high enough to heat 10- to 40-μm capillaries enough to cause purpura. In addition, it is likely that the surrounding tissue was heated well enough as well, at least superficially. It can be speculated that the PWS that responded poorly to the treatment with 6 J/cm^2 and cooling were PWS with more deep vessels, so that bulk cooling, contraction, and scatter reduced the effect of the fluence of 6 J/cm^2 with cooling to the point where it could not treat the bulk of the lesion that was located under the purpura. In the two studies mentioned above, CSC was used; therefore, they are not directly similar to the present study.

Third, Ackermann *et al*. showed that PWS on the neck, trunk, arms, or legs yielded a higher mean grade of fading compared with PWS on the head.[30] This corresponds in general with our results, except for the PWS on the legs and, in one patient, at the neck, which may be due to the above mentioned reasons.

In the study of Chang and Nelson,[20] only PWS with severity score 2 responded better to higher fluences. A possible explanation may be the fact that they have deeper vessels that are not as affected by superficial cooling as less deep vessels.

Due to the relatively small number of participants and standardized fluence parameters, our study merely indicates a tendency. A larger patient population and more elaborate examination methods are necessary to substantiate our assumptions. Differently from Chang and Nelson, we have chosen a prospective, direct side-by-side study design.

In the present study, as in our former studies, we had a nearly unchanged rate of side-effects with 9 J/cm^2, which was due to CAC. The painfulness of the laser pulses was lowered from 6.6 (without cooling) to 4.3 (with cooling) using the same fluence and to 5.3 (with cooling) using a higher fluence (9 J/cm^2). The healing period of postoperative purpura and crusting was 10 to 12 days for all areas. Thus far, we can say that the extent and the duration of purpura and crusting decreased with the use of CAC.[14,15,17] In deviation of the study protocol of 2001, we chose a cooling level of 4 instead of 6, which can be mentioned as an explication for the slightly prolonged healing period of purpura and crusting, especially in area 3.

It is interesting that the augmentation of the fluence to 9 J/cm^2 led to an improved clearance mostly with red PWS. Maybe, other pulse durations, wavelengths, and spot sizes are necessary for other PWS colours.

Conclusion

In our study, we observed a slight but not statistically relevant increase of clearance when using higher fluences and CAC compared with lower fluences without CAC. Because the pain is lowered significantly by using CAC, and because this makes the treatment more comfortable for the patients, we tend to recommend the use of higher fluences (9 J/cm^2) with simultaneous CAC for treating PWS.

References

1 Ashinoff R, Geronemus RG. Flashlamp-pumped pulsed dye laser for port-wine stains in infancy: earlier versus later treatment. *J Am Acad Dermatol* 1991; **24**: 467–472.
2 Fiskerstrand EJ, Svaasand LO, Kopstad G, Ryggen K, Aase S. Photothermally induced vessel–wall necrosis after pulsed dye laser treatment: lack of response in port-wine stains

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with small sized of deeply located vessels. *J Invest Dermatol* 1996; **107**: 671–675.
3 van der Horst CM, Koster PH, de Borgie CA, Bossuyt PM, van Gemert MJ. Effect of the timing of treatment of port-wine stains with the flash-lamp-pumped pulsed-dye laser. *N Engl J Med* 1998; **338**: 1028–1033.
4 Katugampola GA, Lanigan SW. Five years' experience of treating port wine stains with the flashlamp-pumped pulsed dye laser. *Br J Dermatol* 1997; **137**: 750–754.
5 Morelli JG, Weston WL, Huff JC, Yohn JJ. Initial lesion size as a predictive factor in determining the response of port-wine stains in children treated with the pulsed dye laser. *Arch Pediatr Adolesc Med* 1995; **149**: 1142–1144.
6 Nguyen CM, Yohn JJ, Huff JC, Weston WL, Morelli JG. Facial port wine stains in childhood. prediction of the rate of improvement as a function of the age of the patient, size and location of the port wine stain and the number of treatments with the pulsed dye (585 nm) laser. *Br J Dermatol* 1998; **138**: 821–825.
7 Renfro L, Geronemus RG. Anatomical differences of port-wine stains in response to treatment with the pulsed dye laser. *Arch Dermatol* 1993; **129**: 182–188.
8 Yohn JJ, Aeling JL, Walsh P, Morelli JG. Lesion size is a factor for determining the rate of port-wine stain clearing following pulsed dye laser treatment in adults. *Cutis* 1997; **59**: 267–270.
9 Orten SS, Waner M, Flock S, Roberson PK, Kincannon J. Port-wine stains. An assessment of 5 years of treatment. *Arch Otolaryngol Head Neck Surg* 1996; **122**: 1174–1179.
10 Wimmershoff MB, Wenig M, Hohenleutner U, Landthaler M. Treatment of port wine stains with the flash lamp pumped pulsed dye laser. Five years of clinical experience. *Hautarzt* 2001; **52**: 1011–1015.
11 Bencini PL. The multilayer technique: a new and fast approach for flashlamp-pumped pulsed (FLPP) dye laser treatment of port-wine stains (preliminary reports). *Dermatol Surg* 1999; **25**: 786–789.
12 Chang CJ, Kelly KM, van Gemert MJ, Nelson JS. Comparing the effectiveness of 585-nm vs. 595-nm wavelength pulsed dye laser treatment of port wine stains in conjunction with cryogen spray cooling. *Lasers Surg Med* 2002; **31**: 352–358.
13 Edstrom DW, Ros AM. The treatment of port-wine stains with the pulsed dye laser at 600 nm. *Br J Dermatol* 1997; **136**: 360–363.
14 Greve B, Hammes S, Raulin C. The effect of cold air cooling on 585 nm pulsed dye laser treatment of port-wine stains. *Dermatol Surg* 2001; **27**: 633–636.
15 Greve B, Raulin C. Prospective study of port wine stain treatment with dye laser: comparison of two wavelengths (585 nm vs. 595 nm) and two pulse durations (0.5 milliseconds vs. 20 milliseconds). *Lasers Surg Med* 2004; **34**: 168–173.
16 Lou WW, Geronemus RG. Treatment of port-wine stain by variable pulse width pulsed dye laser with cryogen spray: a preliminary study. *Dermatol Surg* 2001; **27**: 963–965.
17 Raulin C, Greve B, Hammes S. Cold air in laser therapy: first experiences with a new cooling system. *Lasers Surg Med* 2000; **27**: 404–410.
18 Scherer K, Lorenz S, Wimmershoff M, Landthaler M, Hohenleutner U. Both the flashlamp-pumped dye laser and the long-pulsed tunable dye laser can improve results in port-wine stains. *Br J Dermatol* 2001; **145**: 79–88.
19 Tanghetti E, Sierra RA, Sherr EA, Mirkov M. Evaluation of pulse-duration on purpuric threshold using extended pulse pulsed dye laser (Cynosure V-star). *Lasers Surg Med* 2002; **31**: 363–366.
20 Chang CJ, Nelson JS. Cryogen spray cooling and higher fluence pulsed dye laser treatment improve port-wine stain clearance while minimizing epidermal damage. *Dermatol Surg* 1999; **25**: 767–772.
21 Chiu CH, Chan HH, Ho WS, Yeung CK, Nelson JS. Prospective study of pulsed dye laser in conjunction with cryogen spray cooling for treatment of port wine stains in Chinese patients. *Dermatol Surg* 2003; **29**: 909–915.
22 Fitzpatrick TB. The validity and practicability of sun reactive skin types2 through VI. *Arch Dermatol* 1988; **124**: 869–871.
23 Andersson RR, Parrish JA. Selective photothermolysis: precise microsurgery by selective absorption of pulsed radiation. *Science* 1983; **220**: 524–527.
24 Anvari B, Tanenbaum BS, Milner TE, Kimel S, Svaasand LO, Nelson JS. A theoretical study of the thermal response of skin to cryogen spray cooling and pulsed laser irradiation: implications for treatment of port wine stain birthmarks. *Phys Med Biol* 1995; **40**: 1451–1465.
25 Nelson JS, Miller TE, Anvari B *et al*. Dynamic epidermal cooling during pulsed laser treatment of port wine stains. *Arch Dermatol* 1995; **131**: 695–700.
26 Pfefer TJ, Smithies DJ, Milner TE, van Gemert MJ, Nelson JS, Welch AJ. Bioheat transfer analysis of cryogen spray cooling during laser treatment of port wine stains. *Lasers Surg Med* 2000; **26**: 145–157.
27 Tunnell JW, Chang DW, Johnston C *et al*. Effects of cryogen spray cooling and high radiant exposures on selective vascular injury during laser irradiation of human skin. *Arch Dermatol* 2003; **139**: 743–750.
28 Tunnell JW, Nelson JS, Torres JH, Anvari B. Epidermal protection with cryogen spray cooling during high fluence pulsed dye laser irradiation: an ex vivo study. *Lasers Surg Med* 2000; **27**: 373–383.
29 Verkruysse W, Majaron B, Tanenbaum BS, Nelson JS. Optimal cryogen spray cooling parameters for pulsed laser treatment of port wine stains. *Lasers Surg Med* 2000; **27**: 165–170.
30 Ackermann G, Hartmann M, Scherer K *et al*. Correlations between light penetration into skin and the therapeutic outcome following laser therapy of port-wine stains. *Lasers Med Sci* 2002; **17**: 70–78.

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