Effect of a Single Application of Pulsed Dye Laser Treatment of Port-wine Birthmarks on Intraocular Pressure

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Background: A new pathophysiologic mechanism has been proposed that indicates that periorbital port-wine birthmarks (PWBs) serve as alternate collateral blood passageways when orbital venous drainage is impaired. The occlusion of such collateral venous channels could, therefore, potentially exacerbate impaired ocular venous flow and trigger the development or worsening of glaucoma in patients with Sturge-Weber syndrome. We investigated to what extent a single application of laser therapy, which occludes only the most superficial portions of a facial PWB, might affect intraocular pressure. Pressures before and after laser treatment were measured to determine pressure difference in 15 patients receiving laser treatment.

Observations: The greatest pressure differences were observed in patients with a PWB closest to the eye (P = .02). Posttreatment pressures were significantly decreased, relative to pretreatment pressures, only in patients with a PWB on the eyelid compared with patients with a facial PWB not near the eyes (2.33 vs 0.75 mm Hg; P = .004). No correlation was found between change in pressure and patient age, PWB size, or number of previous treatments.

Conclusions: A single laser application to a PWB does not appear to show a clinically relevant change in intraocular pressure. Further study is needed longitudinally in a broad range of patients.

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Methods

This was a single-center, retrospective study involving patients with PWBs who were seen for PDL treatment at the Johns Hopkins Outpatient Center, or later at the Johns Hopkins Harriet Lane Clinic, Baltimore, Maryland, from July 31, 2006, to August 28, 2006, and July 2, 2007, to July 30, 2007. The same PDL was used (V-Star Pulsed Dye Laser; Cynosure Inc, Westford, Massachusetts) for all subjects in this study. Patients were eligible for the study if they had a facial PWB and had their eye pressures checked before and after treatment as part of patient care. Patients were included regardless of age, history of treatments, or whether they had a diagnosis of Sturge-Weber syndrome (SWS). Institutional review board approval was given for this study.

Patients typically applied topical anesthetic ointment (lidocaine, 15%; prilocaine, 5%; and phenylephrine, 0.25%) to their PWB 2 hours before laser treatment. Once the patient was in the laser treatment room, 2 procaïnamide anesthetic eye drops were placed in each eye. With the patient sitting upright (so as to simulate pressure readings as taken in an ophthalmologist’s office), a handheld automated applanation tonometer (Tonopen; Mentor Ophthalmics Inc, Norwell, Massachusetts) was used to take 3 pretreatment...
intraocular pressure readings for each eye. Measurements were recorded, and all had a less than 5% error variance as indicated by the device’s digital readout. Protective shielding was then placed over the patient’s eyes. All 3 groups received similar protective shielding during the laser treatments. An episcleral eye shield or metal contact lens was not used on any of the patients. In the case of an eyelid PWB, an external eye shield was used for a facial PWB, and laser therapy was performed by shifting the eye shield out of the field of laser treatment. The patient underwent PDL treatment of the PWB, with all laser specifications recorded. Our usual pulse duration is set at 2 milliseconds (ms) for patients with type 1 or 2 skin and slightly longer with increasing Fitzpatrick skin types but not usually longer than 6 or 10 ms. Since most of our treated patients have type 1 or 2 skin, the majority of our subjects were treated at 2 ms. Immediately following laser treatment, with the patient again sitting upright and the protective shielding removed, the applanation tonometer was used to measure another 3 posttreatment pressure readings in each eye, all with less than 5% error variance. Depending on the size of the PWB and the length of time that had passed between the first pressure check and the second one, anesthetic eye drops may have been reapplied. Pressure measurements were taken by the same individual (S.Y.Q.) both before and after treatment.

We created a deidentified database for review by collecting data from the medical records of each visit. Data collected included the following: age of patient at time of visit; characteristics of the PWB including size, location, color, and appearance; the total energy applied during laser treatment; and number of previous laser treatments. Because the data sets were not normally distributed, nonparametric analyses were used and the data was analyzed with SPSS 15.0 software (SPSS Inc, Chicago, Illinois). A total of 13 subjects (or 30 eyes) were studied. A database was set up with both mean and lowest pressure differences (posttreatment minus pretreatment pressure; a negative number means that the pressure was decreased after laser treatment relative to the pretreatment pressure). The location of the PWB was designated into the following 3 groups in terms of location in relation to each eye: (1) involving the eyelid of the eye being measured; (2) near the eyes but not involving the eyelid of the eye being measured (defined as the border of the PWB closest to the eye being within 2 cm of the lid margin but not involving the eyelid itself); and (3) on the face but not near the eyes.

**RESULTS**

Data from 15 subjects (10 female; median age, 16 years [range, 5-73 years]) were collected (Table). The mean standard deviation of the pressure measurements (3 measurements per eye) was 1.3 mm Hg (range, 0-2.5 mm Hg) before treatment and 1.5 mm Hg (range, 0-4 mm Hg) after treatment. The results did not differ whether the mean pressures or lowest pressures were used for the calculations; the difference in mean pressures is reported herein.

Kruskal-Wallis analysis of all 30 eyes showed a significant effect of PWB location on the change in mean intraocular pressures, post–laser treatment minus pre–laser treatment measurements ($P=0.02$; Figure 1). The closer the eye being measured is to the treated PWB, the greater the impact on the difference in intraocular pressure.

In the eyes with a PWB on the eyelid (n=8), the posttreatment intraocular pressure was decreased relative to the pre–laser treatment pressure by a median amount of 2.33 mm Hg (range, 0.67 to –7.0 mm Hg). In eyes where the PWB was located on the face but not near eyes (n=14), the median pressure difference was only 0.75 mm Hg (range, 1.67 to –0.67 mm Hg), and this was significantly different compared with the eyes with a PWB not near them ($P<0.01$).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Median (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Port-wine birthmark size, cm²</td>
<td>24 (10-144)</td>
</tr>
<tr>
<td>Wavelength of laser, nm</td>
<td>595 (585-595)</td>
</tr>
<tr>
<td>Spot size, mm</td>
<td>10 (5-10)</td>
</tr>
<tr>
<td>No. of pulses</td>
<td>56 (21-180)</td>
</tr>
<tr>
<td>Pulse duration, milliseconds</td>
<td>6 (2-20)</td>
</tr>
<tr>
<td>Energy fluence, J/cm²</td>
<td>8 (7.00-9.00)</td>
</tr>
<tr>
<td>Total energy, J</td>
<td>192 (70-1182)</td>
</tr>
<tr>
<td>No. of previous treatments</td>
<td>11 (2-31)</td>
</tr>
</tbody>
</table>

Figure 1. Median intraocular pressure difference (post–laser treatment minus pre–laser treatment measurements). Error bars show range. The eyes with a port-wine birthmark (PWB) on the eyelid showed a median drop in intraocular pressure that was significant compared with the eyes with a PWB not near them ($P<0.01$).

No correlation was found in the overall group between the change in intraocular pressure and either the age of the patient (Spearman $r=0.043; P=.82$), the size of the PWB (Spearman $r=0.179; P=.34$), or number of previous treatments (Spearman $r=−0.076; P=.69$).

![Table. Data Recorded From Each Patient Visit](image-url)
The classic manifestations of SWS include a cutaneous PWB, ipsilateral ocular involvement often resulting in glaucoma, and radiologic evidence of brain abnormalities consisting of leptomeningeal enhancement and changes in venous structures. A new hypothesis for the pathophysiologic mechanism for SWS traces this entire constellation of findings to the absence of superficial cortical or bridging veins as the primary insult. Bentson and colleagues first demonstrated via simultaneous bilateral carotid angiography in patients with SWS that centrifugal cerebral venous flow is impeded by a relative lack of superficial cortical veins draining into the dural sinuses. These investigators also proposed that impairment of flow and pooling of blood within the leptomeninges may produce leptomeningeal thickening. The lack of a patent centrifugal venous pathway subsequently results in increased centripetal drainage. Bentson and colleagues also demonstrated this enhanced deep venous drainage system in the form of dilated and tortuous deep medullary and subependymal cerebral veins. Parsa proposed that the increase in deep venous drainage would also raise cavernous sinus pressure. This, in turn, would reduce venous drainage of the orbital veins, including the ophthalmic and facial veins, causing orbital and periorbital venous ectasia and the characteristic upper facial PWBs. Because cortical and orbital veins are all emissary (valveless), permitting bidirectional blood flow, it was hypothesized that obliteration of the superficial PWB by laser treatment may result in a reduction in alternative cerebral venous outflow channels including an exacerbation of ocular hypertension. Specifically, it was proposed that treatment of pericranial and upper facial PWBs might obliterate cutaneous vessels draining the orbit and increase ipsilateral intraocular pressure.

The data presented herein, however, does not show that a single laser treatment raises intraocular pressure in older children and adults who are not laser treatment naive. Somewhat unexpectedly, our data demonstrated lower, rather than higher, intraocular pressures after treatment in the group with eyelid lesions compared with the patients with a PWB not near the eye. This small but statistically significant decrease in intraocular pressure after a single laser treatment of PWB involving the eyelids could hypothetically be attributed to (1) the true treatment effect of a single laser treatment on intraocular pressure immediately after procedure, at least transiently, (2) the effect of anesthetic applied locally to the skin around the eye on intraocular pressure, (3) an effect of some other manipulation of the eye not adequately controlled for in our study, or (4) a compensatory vasodilatation at some other site transiently improving vascular outflow from the eye. We do not see any biological plausibility for a true sustained intraocular pressure-lowering effect. It is also unlikely that the topical anesthetic compound, which contains both vasoconstrictive and vasodilatory agents, applied 2 hours prior to laser treatment would account for a drop in pressure over just a few minutes between the 2 pressure measurements. There has been one study of the effects of topical anesthesia on intraocular pressure measured by applanation tonometry and the effect was negligible. However, the mandatory protective eye shielding, together with the digital manipulations necessary, in particular, when treating eyelid lesions, would cause aqueous egress and transiently lower intraocular pressure.

There are several limitations to this study. Measuring several intraocular pressures in quick succession with the attendant pressure on the cornea can lead to increased aqueous outflow and a lowered intraocular pressure. However, the repeated intraocular pressure measurements were consistent in all 3 groups and therefore would not be expected to result in the decrease in intraocular pressure seen in the group receiving laser treatment around the eye but not in the group receiving laser treatment to the face but not near the eyes. Nevertheless, no controls were included who did not receive treatment, and these would be helpful to include in future studies. Furthermore, we cannot know from this study what the impact on intraocular pressure is days or weeks after the treatment. In most cases a single laser treatment results in only partial lightening of the PWB because it only penetrates approximately 1 mm and the meaningful collateral channels may be deeper. Therefore, further studies are needed to study the impact of several laser treatments on intraocular pressure.

Ultimately, the small number of patients presented herein with a single superficial laser application does not allow us to draw decisive conclusions about the potential for more extended laser treatments to have an impact on intraocular pressure over time and ensure safety of the procedure with respect to ocular blood flow and development. We advocate the need for further study (1) in patients with SWS, (2) in infants and young children, (3) in laser treatment–naive patients, and (4) with multiple intraocular pressure measurements over time and after multiple laser treatments when more significant areas and depths of the ectatic venous channels are occluded. We are currently conducting an ongoing retrospective study evaluating the ophthalmologic records of children with SWS during courses of laser treatment that should provide additional information to guide treatment.
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Author Contributions: Drs Cohen, Comi, and Parsa had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Comi, Parsa, Krakowski, and Cohen. Acquisition of data: Quan, Krakowski, and Cohen. Analysis and interpretation of data: Comi, Irving, and Cohen. Drafting of the manuscript: Quan, Irving, and Cohen. Critical revision of the manuscript for important intellectual content: Comi, Parsa, Krakowski, and Cohen. Statistical analysis: Comi. Administrative, technical, and material support: Irving. Study supervision: Krakowski and Cohen.

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REFERENCES


Notable Notes

Tom Sawyer on the Cause and Treatment of Warts

One hundred years ago, America mourned the loss of a great author, Mark Twain (1835–1910). As a tribute to Twain, I composed the following “interview” with one of his most famous characters, Tom Sawyer. Tom Sawyer has now grown up, has graduated college, and speaks a more formal English that is mixed with his old Pike County dialect.

Question 1: Tom, why did you give this interview for the Archives of Dermatology?

Tom Sawyer: The reason is becuz of what is said in chapter 6 of The Adventures of Tom Sawyer concerning warts.1 There I mention that the reason I always got considerable many warts was from playing with frogs so much. I reckon I owe an apology to those frogs becuz they don’t cause no warts, even though they got bumpy heads. Only back then we didn’t know about viruses and how they are really the cause of warts.

Question 2: Can you tell us about your favorite treatment for warts?

Tom Sawyer: My favorite cure for warts is spunk-water, that’s rainwater in a rotten tree stump. Sometimes I take ’em off with a bean.1 My good friend Huckleberry Finn liked to use dead cats to cure warts with. Boy, that wart cure sure got Huck and me into a heap of trouble. Well, to cure warts you have to take the cat and get in the graveyard and that’s what we did. Only then we got to see Injun Joe kill that poor Dr Robinson, which then led us to having all those exciting adventures that Mr Twain wrote about in Tom Sawyer.

Well, me and Huck’s cures for warts were probably more than mere superstitious rituals. For us, they really worked. Nowadays, warts in children can be successfully treated using hypnosis and placebo therapies.2-4 You see, when doctors and patients trust one another and believe something will work, well then, cures, I reckon, are more likely to happen.

Question 3: Do you have any final messages for readers?

Tom Sawyer: It’s nice to know that people still enjoy reading about me and Huck Finn. I want to express my deep appreciation to Samuel Langhorne Clemens, you know, Mr Mark Twain, for writing all those adventures about us. I know that doctor’s serious business and that there are still plenty of warts out there that need curing. And if you’re having trouble getting rid of them, remember old Tom and Huck’s cure: take your dead cat long about midnight to the graveyard when somebody that was wicked has been buried. A devil will come, or maybe two or three, and when they’re taking that fellow away, you heave your cat after ‘em and say, “Devil follow corpse, cat follow devil, warts follow cat, I’m done with ye!” That’ll letch any wart.1

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