Laser Treatment of Port Wine Stains

Description

Port wine stains are common vascular malformations that start as pink macules and, if untreated, tend to become darker and thicker over time. They usually occur on the face and neck, but can be located elsewhere on the body. Treatment with lasers (including pulsed dye lasers, Alexandrite, Nd:YAG lasers and intense pulsed light [IPL]) is proposed.

Background

Port wine stains are the most common of the vascular malformations, affecting approximately 3 in 1,000 children. They are composed of networks of ectatic vessels and primarily involve the papillary dermis. Unlike many other birthmarks, port wine stains do not resolve spontaneously. In contrast, they typically begin as pink macules and become redder and thicker over time due to decreased sympathetic innervation. The depth of the skin lesions ranges from about 1 to 5 mm. Port wine stains are generally located on the face and neck but can occur in other locations such as the trunk or limbs.

Prior to the availability of laser treatment in the 1980s, there were no effective therapies for port wine stains. A laser is a highly focused beam of light that is converted to heat when absorbed by pigmented skin lesions. Several types of lasers have been used to treat port wine stains. Currently, the most common in clinical practice is the pulsed dye laser (PDL), which uses yellow light wavelengths (585-600 nm) that selectively target both oxyhemoglobin and deoxyhemoglobin. Pulsed dye lasers penetrate up to 2 mm in the skin. Newborns and young children, who have thinner skin, tend to respond well to this type of laser; the response in thicker and darker lesions may be lower. Other types of lasers with greater tissue penetration and weaker hemoglobin absorption are used for hypertrophic and resistant port wine stains. In particular, alternatives to the PDL are the long-pulsed 1,064 nm Nd:YAG and 755 nm pulsed Alexandrite lasers. The 1,064 nm Nd:YAG laser requires a substantial degree of skill to use to avoid scarring. Carbon dioxide and argon lasers are relatively non-selective; they were some of the first lasers used to treat port wine stains but were associated with an increased incidence of scarring and are not currently used frequently in clinical practice to treat port wine stains. Intense pulsed light (IPL) devices emit polychromatic high-intensity pulsed light. Pulse duration is in the millisecond range, and devices use an emission spectrum ranging from 500 to 1,400 nm. Compared to other types of lasers, IPL devices include both the oxyhemoglobin selective wavelengths emitted by PDL systems and longer wavelengths that allow deeper penetration into the dermis.
Regulatory Status

Several laser systems have been cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process for a variety of dermatologic indications, including treatment of port wine stains. Approved lasers for this indication include the Candela® pulsed dye laser system (Candela Corp.; Wayland, MA), the Cynosure Photogenica® pulsed dye laser (Cynosure Inc; Westford, MA), and the Cynosure Nd:YAG laser system. In addition, the Cynergy Multiplex Laser (Cynosure), a combined Nd:YAG and pulsed dye laser was approved by the FDA in 2005 for treatment of benign vascular and vascular dependant lesions, including port wine stains.

In 2003, the Lumenis® family of intense pulsed light systems was approved by the FDA; indications for use include dermatologic applications. Subsequently, the NannoLight® intense pulsed light system (Global USA Distribution) was approved by the FDA in 2008 and the Mediflash3 and Esterflash3 systems (Dermeo) were approved in 2010 for indications specifically including treatment of port wine stains.

Policy

*This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Laser treatment of port wine stains in the presence of functional impairment related to the port wine stains may be considered *medically necessary*.

Treatment of port wine stains with lasers in combination with photodynamic therapy or topical angiogenesis inhibitors is considered *investigational*.

Policy Guidelines

Performance of a prior spot test is necessary to select suitable candidates for treatment and to determine the degree of scarring that may occur.

The size of the lesion may require more than one treatment.

Rationale

**Laser treatment monotherapy**

In 2011, a Cochrane review of trials on light or laser sources for treating port-wine stains was published by Faurschou and colleagues. (1) The review included randomized controlled trials (RCTs) comparing any laser or light source to any comparison intervention. Five RCTs with a total of 103 participants met inclusion criteria. The investigators reported that interventions and outcomes were too heterogenous for a meta-analysis of study findings. All studies used a within-participant (e.g., split-side) design and none of them included a sham treatment or no treatment group. Interventions in all of the trials were between 1 and 3 treatment sessions and all trials followed patients for less than 6 months' follow-up. A primary efficacy outcome of the review was reduction in redness; investigators judged that a reduction of more than 20% would represent a clinically relevant effect. In all of the 5
trials, treatment with the pulsed dye laser (PDL) resulted in more than 25% reduction in redness in 50-100% of participants, depending on setting of the laser device. In addition, intense pulsed light (IPL) and the Nd:YAG laser also led to a reduction in redness in 1 trial each. The trials found that long-term adverse effects of laser and light treatment were rare; only 1 participant in 1 trial experienced scarring of the skin and this person had a too-high dose of the Nd:YAG laser. The authors concluded that the evidence supports the use of the PDL as the treatment of choice for port-wine stains.

Representative RCTs included in the Cochrane review and published more recently that evaluated laser treatment of port wine stains are described below:

In 2009, Faurschou and colleagues in Denmark published a study with 20 patients with port wine stains. (2) Port wine stains were on the face (n=15), trunk (n=4), or extremities (n=1). Eight (40%) had previously untreated lesions, and the remainder were previously treated, but with types of lasers not under investigation in the study. Patients received one treatment with a PDL on a randomly selected side of the lesion (left/lower or right/upper) and intense pulsed light (IPL) treatment on the other side. Blinded assessment 12 weeks’ post-treatment found a median of 65% percentage lightening on the PDL side and 30% on the IPL side (p<0.0003). Fifteen (75%) of 20 patients had more than 70% lightening with PDL treatment compared to 6 (30%) in the IPL group; this difference was also statistically significant, p=0.014.

A 2010 study in Germany by Babilas and colleagues was a split-face comparison of PDL and IPL treatment in 25 patients; 11 (40%) had previously untreated port wine stains, and the other 14 had received previous laser treatment. (3) Port wine stains were located in the face and neck region in 18 patients, the trunk in 3 patients, and the extremities in 4 patients. The previously untreated patients were treated with IPL, short-PDL (585 nm and 0.45 millisecond pulse duration), and long-PDL (584-600 nm and 1.5 millisecond pulse duration). Patients who previously failed either short- or long-PDLs did not receive that type of treatment. Blinded outcome assessment was done 6 weeks after treatment. In the treatment-naïve group, assessors rated lightening as excellent (at least 75%) or good (51-75%) in at least one test spot in 7 of 11 (64%) patients after IPL treatment, 5 of 11 (45%) after long-PDL, and 1 of 11 (9%) after short-PDL (between group p-value was not reported). In the group that had been previously treated, lightening was rated as excellent or good in at least one test spot in 4 of 14 (29%) patients after IPL treatment, 1 of 14 (7%) after long-PDL treatment, and 0 (0%) after short-PDL treatment.

In 2012, Klein and colleagues in Germany published findings of an RCT evaluating treatment with a diode laser augmented by the dye indocyanine green. (4) The study included 31 patients with port wine stains. Two areas of 2 by 2 cm were selected in each patient’s port wine stain. The areas were randomly assigned to receive treatment with a PDL or with an indocyanine green-augmented diode laser (ICG + DL). The cosmetic appearance of the lesions was assessed using a 5-point Likert-type scale with 0=no clearance to 4=excellent clearance. Three months after treatment, the mean investigator-rated clearance score was 0.89 (standard deviation [SD]: 0.99) for lesions receiving PDL treatment and 1.30 (SD: 1.29) for lesions receiving ICG + DL treatment. The difference in scores between groups was not statistically significant, p=0.11. At 3 months, patients rated the clearance level as a mean of 0.89 (SD: 0.88) after PDL treatment and 1.71 (SD: 1.24) after ICG + DL, p=0.004. Two patients in the diode laser treatment group experienced adverse events. There was one case of site-specific pain during ICG + DL treatment (8 on a 10-point scale) and 1 case of an atrophic scar.
measuring 5 mm in diameter. Other side effects were burning (PDL: 58%, ICG + DL: 68%), edema (PDL: 3%, ICG + DL: 10%) and purpura (PLD: 71%, ICG + DL, 42%).

**Combination treatment**

Two RCTs on laser treatment in combination with topical angiogenesis inhibitors were identified, and these trials had mixed findings. A 2013 RCT by Passeron et al included 22 children between the ages of 6 months and 18 years who had facial port wine stains no more than 100cm². Patients were randomized to receive PDL alone or laser followed by topical timolol. All patients received 3 laser sessions, with a month between sessions. For patients in the combination treatment group, timolol gel was applied twice daily beginning on the day of the first laser treatment and continuing until 15 days after the third and final treatment. Blinded evaluation of patients occurred at baseline and 1 month after the third laser session. In an intention-to-treat analysis, there was no statistically significant difference between groups in the clinical success rate of the 2 treatments, as measured by an investigator global assessment variable. This variable ranged from -1, worsening, to 4, complete clearance. A score of 3 (marked improvement) or 4 (complete clearance) was given to 1 of 10 patients treated with laser and 2 of 12 patients treated with combination therapy, p=1.0.

A 2012 study by Tremaine et al evaluated PDL treatment with and without the addition of imiquimod cream. The study included 24 subjects with port wine stains. All patients initially received 1 session of laser treatment. Five patients enrolled in the study twice, with a washout period of at least 4 weeks before re-enrollment. Patients were randomized to receive additional treatment with either 5% imiquimod cream or placebo cream, to be applied 3 times a week for 8 weeks, beginning the day following laser treatment. Chromameter measurements were taken at baseline and at 8 weeks after laser treatment. The primary outcomes were change in erythema (defined as red/green color saturation with values ranging from +60 green to -60 red) and overall change in 3 color dimensions (reflected light intensity, green/red color saturation, and blue/yellow color saturation). The mean change in erythema was 0.43 (SD=1.63 for the laser plus placebo sites and 1.27 (SD=1.76) for the laser plus imiquimod sites. The difference between groups was statistically significant (p=0.03) and favored combined treatment. Similarly, the mean change in overall color was 2.59 (SD=1.54) for laser plus placebo and 4.08 (SD=3.39) for laser plus imiquimod, p=0.04.

**Practice Guidelines and Position Statements**

None identified.

**Summary**

Studies have generally found that laser treatment can be effective at lightening port wine stains. Therefore, laser treatment of port wine stains is considered **medically necessary**. The preponderance of evidence is on the pulsed dye laser; there is insufficient evidence from comparative studies that one type of laser results in more lightening than another.

The use of laser therapy in combination with an angiogenesis inhibitor treatment has not been validated and is considered **investigational**. Angiogenesis inhibitor agents are not FDA approved for treatment of port wine stains. There is evidence from one small RCT that combined treatment with
pulsed dye laser combined with a topical angiogenesis inhibitor is superior to PDL treatment alone; additional trials confirming these findings are needed.

**Medicare National Coverage**

No national coverage determination.

**References**


**Policy History**

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<td>Rationale and References Updated</td>
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<tr>
<td>December 2012</td>
<td>Update Policy</td>
<td>Policy updated with literature search, reference 4 added. Other references removed or renumbered.</td>
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Signature on File
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