

Original research article

Lasers for treatment of hemangiomas: A review

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Abstract

Hemangiomas are one of the most common tumors of childhood. Treatment can be sought for a variety of reasons like pain, ulceration, bleeding and disfigurement. Hemangiomas can be treated by oral and topical beta blockers, corticosteroids, cryotherapy, surgery and lasers. A systemic review of the literature was performed to collect data about various lasers used to treat hemangiomas. There have been many reports of the treatment of these lesions using different types of lasers such as argon laser, Neodymium: Yttrium-Aluminum-Garnet (Nd:YAG) laser, carbon dioxide laser, Potassium titanyl phosphate (KTP), pulsed dye laser (PDL), long-pulsed tunable dye laser and intense pulsed light (IPL) with good results and minimal side-effects.

Keywords: Laser, hemangioma, therapy, pulsed dye laser, intense pulsed light

Introduction

Hemangiomas are one of the most common tumors in childhood. Some of the risk factors associated with hemangioma are low birth weight, prematurity, multiple gestation and female sex^[1].

There are two types of hemangiomas namely congenital hemangioma (CH) and infantile hemangioma (IH). Infantile hemangiomas usually appears after birth and have a phase of rapid growth followed by involution. IH mostly occur in the head and neck region^[2]. The CH is present since birth. The CH can either be Rapidly Involuting Congenital Hemangiomas (RICH) or Non Involuting Congenital Hemangioma (NICH)^[3]. As suggested by name RICH undergo rapid involution and NICH do not involute. RICH usually do not require any treatment.

Characteristic clinical course of infantile hemangioma consists of following stages^[4,5,6].

- a. **Nascent stage:** It is the stage where lesion has not yet appeared. Sometimes erythema may be present. Usually lasts for 1 to 3 months.
- b. **Proliferative stage:** Proliferation of lesion occurs over next 6 to 10 months. It consists of a period of early rapid growth followed by late slow growth. Most of the lesions reach their maximum growth by 9 to 10 months^[4].
- c. **Plateau stage:** The lesion remains stable for a variable amount of time.
- d. **Involution stage:** Lesion starts to decrease in size. Colour of the lesion may change from bright red to gray or purple. Approximately half of the hemangiomas involute by four years of age^[7]. A residual fibro-fatty tissue can be seen in 40-50% of lesion after involution is complete.

Some hemangiomas do not undergo proliferation and are considered to be in abortive phase.

Treatment of hemangiomas

Hemangiomas are one of the most common tumors of childhood. In a study of 121 infants conducted by Batta *et al.* it was observed that for uncomplicated hemangiomas laser treatment offer no better results that wait and watch approach. In their study about 42% infants had lesions cleared by 1 year of age without any therapy^[8]. Treatment can be sought for a variety of reasons like pain, ulceration, bleeding, and disfigurement. Hemangiomas can be treated by oral and topical beta blockers, corticosteroids, cryotherapy, surgery and lasers.

Systemic steroids

Systemic steroids have been effective in treatment of IH. [9, 10] Prednisolone is usually given in dosage of 2–3 mg/kg/day for 3-8 weeks^[9, 10]. Despite being effective its use is limited because of an array of side-effects like growth delay, cushingoid appearance, increased risk of infections and behavioral changes.

Intralesional steroids

Kushner has used intralesional steroids for eyelid hemangiomas and met with varying degree of success^[11, 12]. Triamcinolone and betamethasone have been used for intralesional injection. Response may be drastic and rapid, with improvement in days. There is risk of skin atrophy, pigmentary changes and adrenal suppression.

Topical steroids

Topical steroids like clobetasol propionate, betamethasone dipropionate and halobetasol propionate have been used for treatment of hemangioma^[13, 14, 15]. Even though when used topically it avoids risk of serious effects of systemic and injected steroids, it still can cause side effects like atrophy, glaucoma, hypertrichosis and hypopigmentation when used over time. Topical treatment is found to be effective only for superficial lesions and deep lesions fail to respond well.

Interferon-alpha

Interferon-alfa has been used for its anti-angiogenic properties to treat hemangioma. In one study about 90% of the lesions regressed following its use^[16]. However, it is not accepted as a first line treatment modality because of its neurotoxicity. It can cause serious side effects like neutropenia and spastic diplegia^[16-17].

Vincristine

Vincristine is commonly used in cancer chemotherapy. It is an alkaloid which acts by inhibiting microtubule formation during mitosis. Vincristine has been used for life threatening IH.¹⁸ Because of its various side effects it is not considered as a first line treatment modality for hemangioma. Some of its side effects are hematologic toxicity, constipation and peripheral neuropathy^[19].

Beta-blockers

Leaute-Labreze *et al.* serendipitously discovered the role of propranolol in treatment of hemangioma. After noticing the regression of nasal tip hemangioma following treatment with oral propranolol given for hypertrophic obstructive cardiomyopathy in an infant, they treated ten more patients with hemangioma with oral propranolol^[20]. It showed good results even in large and deep lesions.

Fay *et al.* and Taban and Goldberg also reported good results in hemangioma following treatment with oral propranolol^[21, 22].

Oral propranolol should be administered to children under close monitoring as it can cause serious side effects like, hypoglycemia, bronchospasm, bradycardia, hypothermia and hypotension.

Topical beta-blockers

Role of topical beta blockers has been explored in treatment of hemangioma in order to reduce side effects caused by oral propranolol. There have been several reports of successful treatment of hemangioma with topical timolol.^[23, 24] None of these cases were associated with any side effects due to medication. Use of topical beta-blockers appears to be safe for long term treatment of superficial lesions.

Beta-blockers appears to act by causing vasoconstriction and inhibition of proangiogenic factors such as vascular endothelial growth factor and basic fibroblast growth factor which reduces the growth of lesion. Proliferating endothelial cells undergo apoptosis resulting in resolution of lesion^[25].

Surgery

Surgery should be considered in lesions which cause significant cosmetic or functional defect and are refractory to less invasive treatments. Surgery should be done only after taking into consideration the size and location of the lesion and the risk surgery possess to the surrounding tissue^[26]. Surgical excision carries the risk of bleeding, damage to surrounding structures and scarring.

Laser treatment

One of the earliest lasers to be used for vascular lesions was argon laser. Even though these lasers were effective their use was limited because of side-effects like scarring and dyspigmentation. Use of lasers as treatment modality for vascular lesions gained momentum after Anderson and Parrish described the theory of selective photothermolysis^[27]. Applying this theory to use physicians were able to greatly reduce the side-effects as they were able to selectively target hemoglobin within blood vessels without damaging the surrounding tissue.

Laser therapy cause damage to blood vessels either by photocoagulation or photomechanical

effects^[28]. Haemoglobin acts as target chromophore for lasers. Hemoglobin absorbs light energy from lasers and convert it into thermal energy. This heat generated cause damage to vessel^[28]. In photomechanical damage the heat causes blood to boil and damaging to vessel wall which result in haemorrhage^[29]. It is evident as purpura after treatment. In photothermal damage the heat generated by absorption of laser energy by hemoglobin cause intravascular coagulation^[29]. It is seen clinically as immediate blanching or darkening of the vessels followed by edema and erythema^[29].

Hemoglobin is the target chromophore in the laser treatment of vascular lesions. It has absorption peaks at 418, 542 and 577 nm^[29, 30]. It also has a peak near-infrared portion of the spectrum (700 to 1100 nm)^[29]. While selecting laser for treatment of vascular lesions in darker skin patients (Fitzpatrick skin phototypes IV to VI) one should prefer laser with longer wavelength as melanin is a competing chromophore at shorter wavelengths^[29]. Melanin can absorb laser energy and result in side-effects like hyperpigmentation or hypopigmentation.

Physician should be careful while selecting the laser parameters. Thermal relaxation time (TRT) of the target tissue helps in selecting appropriate pulse duration. TRT is defined as time required by target tissue to lose about 63% of the incidental thermal energy. It is dependent on the size of target tissue^[31]. Pulse duration more than the TRT of the target tissue will cause damage to the surrounding tissue and increase the chances of side-effects^[28, 29]. For good results with minimal side-effects pulse duration should be less than TRT. Fluence is energy delivered per unit area. It is expressed as joules/cm² ^[31]. More fluence is required for deeper tissue. Bigger spot size allows large area to be covered in small amount of time. Bigger the spot size deeper the penetration^[28, 29]. Appropriate measures of cooling should be used to protect the epidermis. Cooling can be done using ice packs, cryogen spray or chilled sapphire tips.

General considerations for selection of patients

The patients should undergo laser treatment after proper evaluation. The patients should be counseled about the possible effects and side effects of the procedure. It should be explained to them in their vernacular language. Written informed consent should be taken from every patient before starting the treatment.

Patients with unrealistic expectations, pregnant and lactating females, patients with connective tissue disorders, psoriasis, vitiligo, bleeding disorders, active local infection and keloidal tendencies should not be considered for laser treatment

Types of vascular lasers

There have been many reports of the treatment of vascular lesions using different types of lasers such as argon laser, Neodymium: Yttrium-Aluminum-Garnet (Nd:YAG) laser, carbon dioxide laser, Potassium titanyl phosphate (KTP), pulsed dye laser (PDL), long-pulsed tunable dye laser and intense pulsed light (IPL) with good results and minimal side-effects. The wavelength of the laser [Table 1], pulse durations and how the target skin tissue absorbs this, determine the clinical applications of the lasers.

Use of many lasers such as copper vapor, krypton and argon has been discontinued because of higher rate of side-effects like scarring and dyschromia ^[28].

Pulsed dye laser

Pulsed dye lasers (PDLs) use a rhodamine dye that is dissolved in a solvent and pumped by a flash lamp. This laser energy is delivered to tissue by fiber optics. PDLs emit wavelengths in the range of 585 to 600 nm with pulse duration of 0.45 to 40 milliseconds. The PDL is considered as the laser of choice for the treatment of port-wine stains and hemangioma. It also gives good results in superficial vascular lesions like rosacea and telangiectasia. Landthaler *et al.* observed that superficial hemangiomas responded very well to PDL treatment, but outcome was poor in case of thick hemangiomas ^[32]. They preferred the Nd:YAG laser over PDL for the treatment of thick hemangiomas.

In a study conducted by Kono *et al.*, long-pulsed dye laser was found to be safer and more effective than PDL in early treatment of childhood hemangiomas^[33].

Hypopigmentation and skin atrophy are side-effects associated with PDL treatment^[8].

Carbon Dioxide Laser

The carbon dioxide (CO₂) laser has a wavelength of 10,600nm. The laser energy is absorbed by the water which quickly heats and vaporizes, thus destroying the tissue structure.

CO₂ laser has been used by Nammour *et al.*, to treat hemangioma. In their study the aesthetic outcome obtained with the CO₂ lasers was significantly better than those obtained by use of Diode or Nd:YAG lasers^[34].

CO₂ laser can also be used to treat the fibro-fatty tissue and atrophic plaques left after the regression of hemangioma^[35]. Brightman *et al.*, used ablative CO₂ laser to treat the fibro-fatty residual of 5 children after the regression of hemangioma^[36]. Improvement was noted in colour, texture and overall appearance by at least 50-75% in the 5 children.

Fractional CO₂ laser has been used to assist drug delivery for enhancing topical timolol permeation into

deep hemangioma^[37].

Edema, erythema, bleeding and crusting are common side-effects noted with CO₂ laser. Sometimes infection and scarring following the procedure can occur.

Neodymium: yttrium-aluminum-garnet (Nd: YAG) laser

Nd: YAG laser has a wavelength of 1064 nm. Because of bigger wavelength it can penetrate deeper. The absorption coefficient of blood at 1064 nm is much higher than that of the surrounding dermis^[38]. This difference in absorption coefficients allows Nd:YAG laser to target deeper vessels without affecting surrounding dermis or epidermis^[38]. Landthaler *et al.*, preferred the Nd: YAG laser over PDL for the treatment of thick hemangiomas^[32]. They also observed superficial scarring in patients treated by Nd:YAG laser. Vlachakis *et al.*, were successfully able to use Nd:YAG laser with minimal side-effects by ice cooling the epidermis^[39]. In a study conducted by Zhong *et al.*, in 794 patients Nd:YAG laser was found to be a safe and effective treatment for IH^[40]. Nd:YAG laser has been found to be effective and safe in a number of other studies as well^[41, 42].

Combined therapy of Nd:YAG laser with PDL has also been found to be effective in treating hemangioma^[43, 44].

Erythema, pain, postoperative bleeding and atrophic scar formation are some of the side-effects noted with Nd:YAG laser.

Potassium titanyl phosphate laser

Potassium titanyl phosphate (KTP) lasers emit a wavelength of 532 nm. Pulse durations range from 1 to 150 milliseconds. It is delivered by optic fibre that can be easily manipulated. KTP lasers are more portable because of smaller size. It is preferentially absorbed by hemoglobin and has a photocoagulation effect on vascular lesions without bleeding^[45]. KTP laser was found to be superior to a hyfrecator in treating vascular spiders and angiomas as fewer sessions were required and because of the lack of side-effects^[46]. KTP lasers have been used for superficial vascular lesions and laryngeal hemangiomas with good results^[47, 48].

The KTP laser is more suitable for patients with Fitzpatrick skin types I to III. Patients with darker skin types are more prone to side-effects. Some of the side-effects associated with KTP laser are swelling, bruising, hypo- or hyperpigmentation, blistering and scabbing^[47].

Intense pulsed light

The intense pulsed light (IPL) is not a laser. IPL flash lamps generate non-coherent and polychromatic light beam with wavelengths in range of 500 to 1200 nm. IPL comes with various cut-off filters which enable it to be used for various lesions. IPL acts by increasing the blood vessel temperature resulting in coagulation and destruction of vascular lesion^[49]. The lesion is then replaced by fibrous granulation tissue^[49].

IPL has a bigger spot size; hence larger areas can be treated efficiently with less discomfort^[50]. For effective treatment, the hand piece must be in contact with the skin to avoid divergence of IPL beam^[51]. Although larger spot size allows better coverage of large areas it also increases the risk of more side effects^[51].

Because of its polychromatic nature and availability different filter settings of the IPL, it can be used for variety of vascular lesions. It can target oxyhemoglobin (predominantly found in clinically red lesions), deoxygenated hemoglobin (predominantly in blue lesions), thus improving the clinical efficacy^[49].

IPL also allows the user the facility to split the energy into two to three pulses with different pulse delays. This provides the skin the time to cool between pulses and results in fewer side-effects^[50].

As per study done by Caucanas *et al.*, IPL appears to be a safe and effective treatment for infants with superficial hemangiomas. IPL with carefully selected parameters was considered a safe and effective modality for hemangiomas. Bleeding, ulceration and crusting were noted as side-effects^[52].

One should be cautious while using IPL in darker skin types as they are more prone for side-effects^[53]. Pain, erythema, hypopigmentation and hyperpigmentation are commonly observed side-effects with IPL.

Conclusion

A variety of lasers are now available for the treatment of hemangioma. Each of these lasers has effects and limitations because of depth of penetration, target chromophore and caliber of vessels targeted. Lasers can be used alone or in combination with other treatment modalities. Complications vary with type of laser, parameters used, site treated and skin types.

Table 1: Types of vascular lasers

Laser	Wavelength emitted
Potassium-titanyl-phosphate (KTP)	532 nm
Pulsed dye laser (PDL)	585/595 nm
QS ruby	694 nm

QS alexandrite	755 nm
Neodymium: Yttrium-Aluminum-Garnet (Nd:YAG)	1064 nm
Erbium: YAG	2490 nm
CO ₂	10,600 nm

Abbreviations

Congenital hemangioma- CH.
 Infantile hemangioma- IH.
 Rapidly Involuting Congenital Hemangiomas- RICH.
 Non Involuting Congenital Hemangioma- NICH.
 Neodymium: Yttrium-Aluminum-Garnet- Nd: YAG.
 Carbon dioxide- CO₂.
 Potassium titanyl phosphate- KTP.
 Pulsed dye laser- PDL.
 Intense pulsed light- IPL.
 Thermal relaxation time- TRT.

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