Innovative: International Multi-disciplinary Journal of Applied Technology
(ISSN 2995-486X) VOLUME 02 ISSUE 03, 2024

Vascular Lesions Treatment by Multiplex Technology

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Abstract:

This project presents an introduction to laser multiplex technology used for treating vascular lesions. This study examines aims to treat port-wine stains more effectively than conventional methods. Both high-powered 585nm pulsed dye laser and 1064nm Nd: YAG laser wavelengths are used to treat two cases of Port-wine stains at early and mature state. The Multiplex technology enables the sequential emission of the two wavelengths from one delivery system for optimized clinical effectiveness.

Keywords: YAG laser, vascular lesions, port-wine stains

Introduction

Vascular lesions were one of the first indications for which lasers were used. In 1963, Goldman used ruby, neodymium-doped yttrium-aluminum-garnet (Nd: YAG), and argon lasers to treat vascular lesions like hemangioma and port-wine stain. Initially, lasers were used only for congenital lesions but later, the indications were extended to the acquired vascular lesions also [1].

Vascular anomalies are one of the most common indications for laser surgeries. If not treated, vascular lesions can often result in disfiguring scars, hemorrhagic episodes, and infections, apart from the severe psychological impact it can cause. The evolution of vascular lasers has a tremendous impact on the management of vascular lesions including hemangiomas, port-wine stain, telangiectasia, erythema, rosacea, and leg veins. The initial argon or ruby lasers though gave a satisfactory color change in many cases, these were often pledged with an unacceptable high rate of complications including disfiguring scarring. With a better understanding of the mechanism of action through selective photothermolysis, more emphasis was given, to selective destruction of the target tissue and minimizing collateral damage; this led to the advent of pulsed laser [2]. Even though present-day vascular lasers are considered an effective and safe modality of treatment, it is important to follow proper guidelines and safe practices to achieve satisfactory results and avoid any untoward reaction. This project focuses on the principles of vascular lasers and the guidelines for patient selection and treatment protocol required for providing safe and effective treatment [1]. The International Society for Study of Vascular Anomalies has classified vascular anomalies into mainly two groups: Vascular tumor: Hemangiomas are vascular tumors that are rarely apparent at birth, grow rapidly during the first 6 months of life, involute with time, and do not necessarily infiltrate, but can sometimes be destructive [3].

Figure (1): Facial Hemangioma.

- Vascular malformations: are irregular vascular networks defined by their particular blood vessel type. In contrast to hemangiomas, they are present at birth, slow-growing, infiltrative, and destructive.

Figure (2): Capillary Malformations of the Face.

Almost all vascular malformations and nearly 40% of hemangiomas eventually require intervention [3]. Overall, port-wine stain and hemangioma are the most. Pulsed dye laser (PDL) is often considered a gold standard of treatment with a wavelength of 585–595 nm achieving great depth of penetration and long variable pulse duration from 0.45 to 40 ms that can treat vascular anomalies of different diameters [4, 5].

The efficacy of PDL is often limited by its inability to penetrate a depth beyond 2 mm. So, other lasers with longer wavelengths, especially alexandrite (755 nm

Spot size for the laser helps to control the amount of energy being delivered to the desired target. Lasers with larger spot sizes penetrate deeper into the tissue as they cause less scattering of energy and deliver more heat to the target tissue leading to thermocoagulation. Similarly, a laser with a smaller spot size causes more scattering of energy and is, therefore, not very effective in thermocoagulation of deeper vessels. Also, an increase in spot size may cause a dramatic increase in the amount of energy delivered to the target tissue if the fluence is not adjusted. Smaller

Fluence is defined as the energy delivered per unit area. It is measured in J/cm2. It is important to manipulate the fluence according to the type of lesion and the area of the body being treated as delivering excessive energy may lead to tissue damage. Various parameters, like vessel color, size and depth of the vessel, and spot size of the laser, should be taken into account while selecting the appropriate fluence [6]. Smaller vessels absorb less energy as they have less amount of chromophore, hence, requiring a higher fluence. Vessels that are blue and purple require less fluence as compared to pink and red vessels, as they absorb more light energy. Vessels in areas of greater intravascular pressure like that of the nose or legs require higher fluences than those with less intravascular pressure [1].The pulse duration required depends on the diameter of the underlying vessel. Vessels with a diameter of 10– 100 μm usually have a thermal relaxation time of 1– 10 ms and will require a shorter pulse duration whereas vessels with a larger diameter, that is more than 100 μm will have a higher thermal relaxation time and hence, will require a longer pulse duration [1].The depth of the underlying blood vessels must be taken into account while choosing the parameters for treatment. Vessels that are located superficially usually respond well to the wavelengths of 577 and 585 nm whereas the vessels lying deeper Laser treatment of vascular lesions is accomplished most often using the principle of selective photothermolysis, using nonablative vascular-selective lasers that target hemoglobin in the vessel. When the appropriate laser and settings are selected and applied, lasers demonstrate success in safely destroying cutaneous vessels of various types, sizes, and depths [2].

Vascular lesions are composed of endothelial cell–lined vessels containing colorless lymphatic fluid, blood-colored by hemoglobin, or both. Vessels vary in diameter, thickness, and depth. Hemoglobin present may be in varying states of oxygenation, including deoxyhemoglobin, oxyhemoglobin, methemoglobin, or any combination of these forms. Selective photothermolysis (Figure 2-1) employs the observation that preferential absorption of a laser pulse by certain pigmented chromophores causes their heating and subsequent thermal destruction, with relative sparing of surrounding structures. Excess thermal energy absorbed by the pigmented target diffuses to surrounding targets in a process termed thermal relaxation. To selectively destroy vessels, the laser wavelength should be preferentially absorbed by the chromophore present in the vessel, which in the case of blood-filled lesions is hemoglobin in varying forms. The wavelength must also be sufficiently long to reach the targeted vessel depth. The pulse duration should be equal to or less than the vessel thermal relaxation time (τr) to avoid heat damage to the surrounding structures. That is, for cylindrical vessels [2]:

$$\tau r = d^2/16\kappa;\ \kappa = 1.3 \times 10^{-3}\ cm^2/s \qquad (2\text{-}1)$$

The energy delivered, or fluence should be sufficient to damage the vessel(s) while also conservative enough to limit injury to surrounding tissue [2].

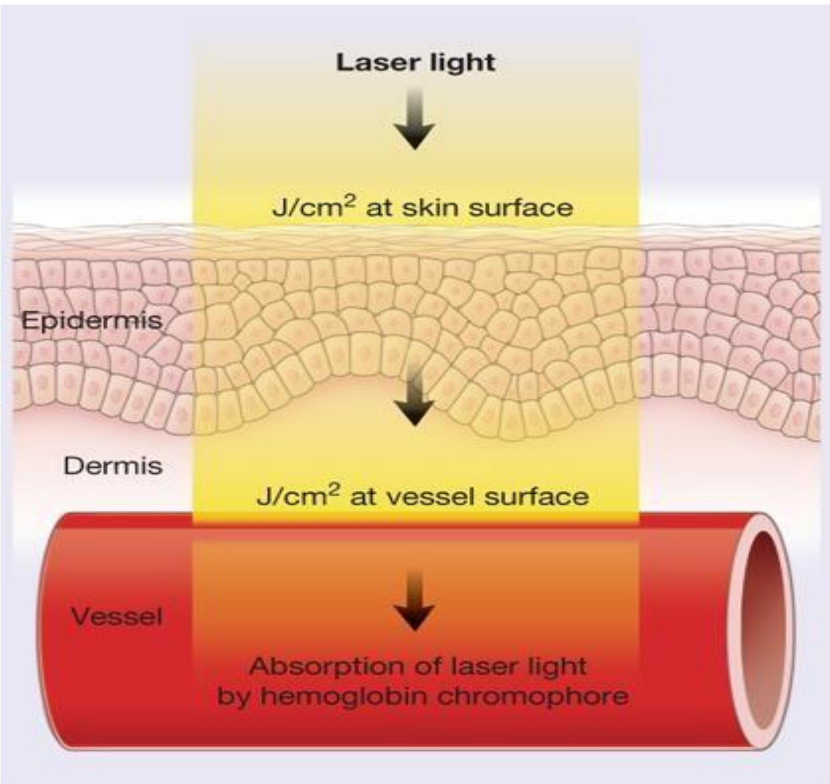

Figure (3): Selective Photothermolysis of Vessels [2].

port-wine stain (PWS) is a vascular lesion composed of ecstatic capillaries and postcapillary venules in the superficial venous plexus. They are a capillary malformation that comprises a variety of distribution (300–600 μm in-depth) and

sizes of blood vessels (10–150 μm). PWS is congenital in most cases but may appear after birth in rare instances. Approximately 0.03% of the newborn babies are affected by port-wine stain and they tend to persist throughout life and increase in thickness with time. A study showed that by the 3rd–5th decade of life, the majority of port wine stains become thickened and at times, nodular as seen in figure (2.2) [8].

The color of PWS may determine the depth of the vessel, pink and purple vessels signify deeper lesions than red. The mean vessel diameter is also different, namely a smaller diameter in pink lesions (mean 16.5 μm) and a larger diameter in purple lesions (mean 51.2 μm) [9].

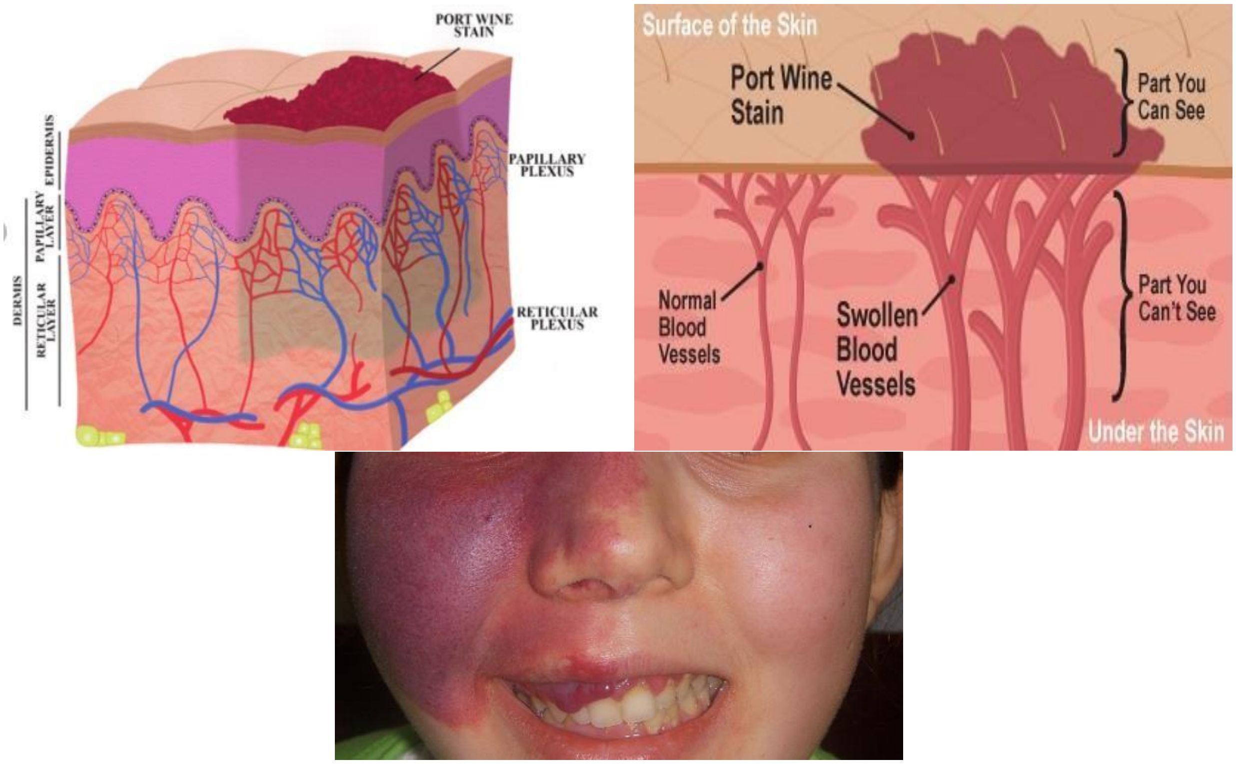

Figure (4): Port Wine Stain [8].

PWS is often complicated with soft tissue overgrowth causing functional impairment and also may cause recurrent bleeding episodes and infection. The vessel size varies considerably from 7 to 300 μm, with older lesions tending to have larger vessel diameters. Port-wine stain can be associated with various syndromes, and before starting laser treatment, one should always eliminate the possibility of associated artery venous malformation [10].Laser Treatment of Port Wine Stain Port-wine stain can be hidden using cosmetic camouflage. It does not take away a port-wine stain but covers it up using a special kind of makeup, which is water- resistant. This is considered to be a cover to the lesion and not a treatment, the only way to treat it is by laser surgery. The treatment of PWS with lasers effectively diminishes redness, thickness, general appearance, the possibility of bleb formation, and psycho-social discomfort. The lasers used in this process are either pulsed dye lasers or Nd: YAG lasers [5]. Pulsed Dye Laser Pulsed dye lasers are lasers that use dyes as an active medium. studies showed the advantages of dye laser that demonstrated a broad tuning range of wavelength up to 100 nm and a wide range of applications. The active medium is usually a liquid solution, which also provides the flexibility of wavelength but degrades over time, figure (2.3) shows a schematic diagram of a dye laser [11].

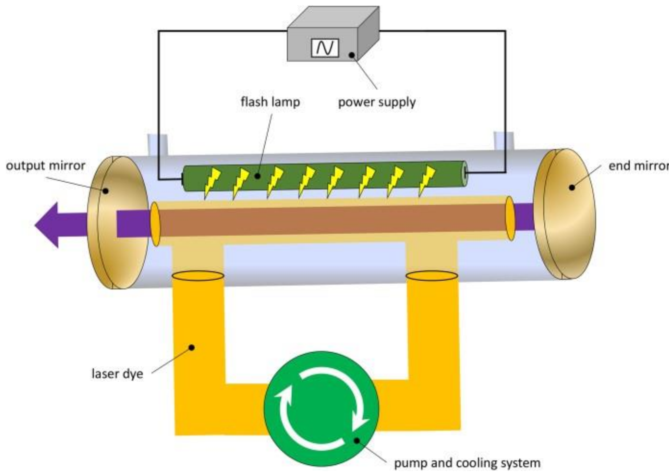

Figure (5): Setup of a Flash Lamp-Pumped Dye Laser.

An external high energy source such as a flash lamp is needed to pump (stimulate emission) the liquid beyond its lasing threshold. The initial pulsed dye laser (PDL) for vascular lesion emitted 577 nm which corresponded to the peak absorption of oxygenated hemoglobin. Later, the available PDLs in the market deliver 585 and 595 nm for better penetration [1]. It is often considered the gold standard of treatment for port-wine stain and is usually successful in improving 80% of the patients. However, only 20% of the patients show complete clearance after a requisite number of sessions. The target chromophore for the vascular lesion is mainly hemoglobin. Oxygenated hemoglobin strongly absorbs visible light at 418, 542, and 577 nm. Deoxygenated hemoglobin (venous blood) selectivity is maximal at 694 nm, and significant at 595, 600, 633, and 755 nm. Methemoglobin is relatively strongly absorbed at 633 nm, which corresponds to the wavelength of PDL available in the market, as shown in[12].The MultiPlex system is considered the most up-to-date laser technology available in the medical field for the treatment of vascular lesions. The laser uses a more intense single-wave light to seal off the dilated blood vessel. It is the first system available that can sequentially emit with rapid succession, two wavelengths from the same fiber-optic – a Pulsed Dye laser (PDL) and an Nd: YAG laser [17]. The adjustable time delay between pulses increases the safety and effectiveness of this laser treatment. This technology minimizes or prevents post-treatment swelling and bruising, side effects frequently present when these lasers are used individually [16]. A long pulse pulse-dye-laser and a high-powered Nd: YAG is combined into one system. These wavelengths were chosen for their absorption characteristics and depth of penetration. Both wavelengths are well absorbed by the blood. Both wavelengths are also absorbed by melanin. The wavelengths are synergistic in their depth of penetration criteria, the PDL has a more shallow depth of penetration while the Nd: YAG penetrates deeper, so it can treat all types of vascular and pigmented lesions including spider veins, and rosacea more effectively than conventional, single-wavelength technology, including: facial and leg telangiectasias; spider veins; hemangiomas; mature and blebbed port wine stains and other vascular malformations; rosacea; scars; and warts [17][18]. Sometimes it's necessary to use both wavelengths to treat the same area at the same time, depending on the indication to be treated. The science behind this procedure is that the pulsed-dye laser fires milliseconds before the Nd: YAG laser. This first pulse converts oxy-hemoglobin to methemoglobin, which increases the absorption coefficient for the Nd: YAG wavelength by 300–500%. Next, the Nd: YAG laser fires and is more effectively absorbed by the converted target, enabling reduced Nd: YAG fluence for enhanced patient safety. Since greater penetration depth is achieved, outcome results are also optimized. By emitting dual wavelengths, safe and effective results in less time than single-wavelength systems are achieved. which means greater comfort and satisfaction [17][18]. Patients experience fewer side effects. It eliminates purpura, a bruising typically associated with older pulsed-dye lasers as well as dramatically reduce the risk of scarring [1][19][20].

Materials and Method

The MultiPlex system is considered the most up-to-date laser technology available in the medical field for the treatment of vascular lesions. The laser uses a more intense single-wave light to seal off the dilated blood vessel. MultiPlex technology is the first system available that can sequentially emit with rapid succession, two wavelengths from the same fiber optic, a Pulsed Dye laser (PDL), and an Nd: YAG laser. The adjustable time delay between pulses increases the safety and effectiveness of this laser treatment. This technology minimizes or prevents post-treatment swelling and bruising, and side effects frequently present when these lasers are used individually. Multiplex technology treats vascular lesions with higher efficacy and minimal side effects. That's because it enables the sequential emission of two wavelengths from the same delivery system a high-powered pulsed-dye laser and a 1064-nm long- pulse Nd: YAG laser. Both wavelengths are indicated for performing vascular- related applications. The pulsed-dye laser is the gold standard for targeting vascular lesions such as port-wine stains. Likewise, the Nd: YAG laser is more effective at treating larger veins. MultiPlex's sequential dual-wavelength technology has been proven more efficacious than single wavelength technology by customizing the time delay between wavelength delivery as seen in figure (6). The pulsed dye laser converts oxy-hemoglobin to methemoglobin and micro-clots increasing absorption of the Nd: YAG wavelength by 300–500 percent and thereby enabling reduced Nd: YAG fluence for enhanced safety. In addition, since greater absorption and penetration depth is achieved, outcome results are optimized as seen in figure (7).

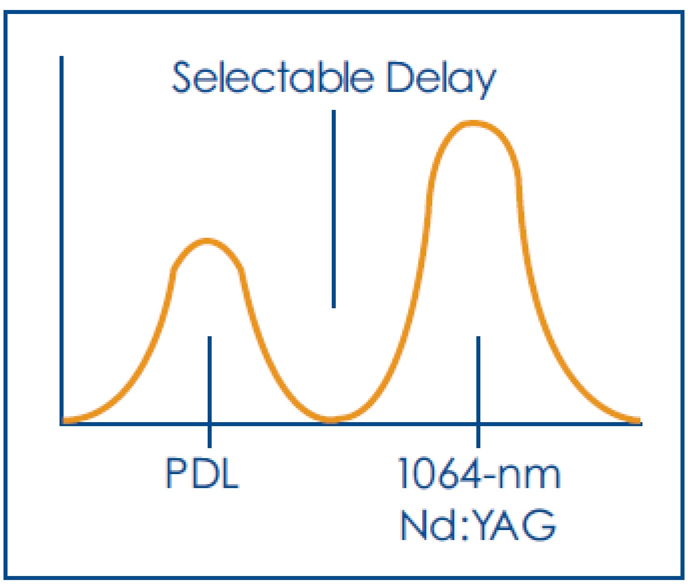

Figure (6): Time Delay Between Wavelengths.

Multiplex technology offers fewer side effects. It virtually eliminates purpura, a bruising typically associated with pulsed-dye lasers, as well as dramatically reduces the risk of scarring. Emitting dual wavelengths provide safer and more effective results in less time than single-wavelength systems. that means greater comfort and satisfaction. To further enhance the patient's comfort and decrease the likelihood of adverse side effects, laser treatment is carried out with an adequate air cooling system.

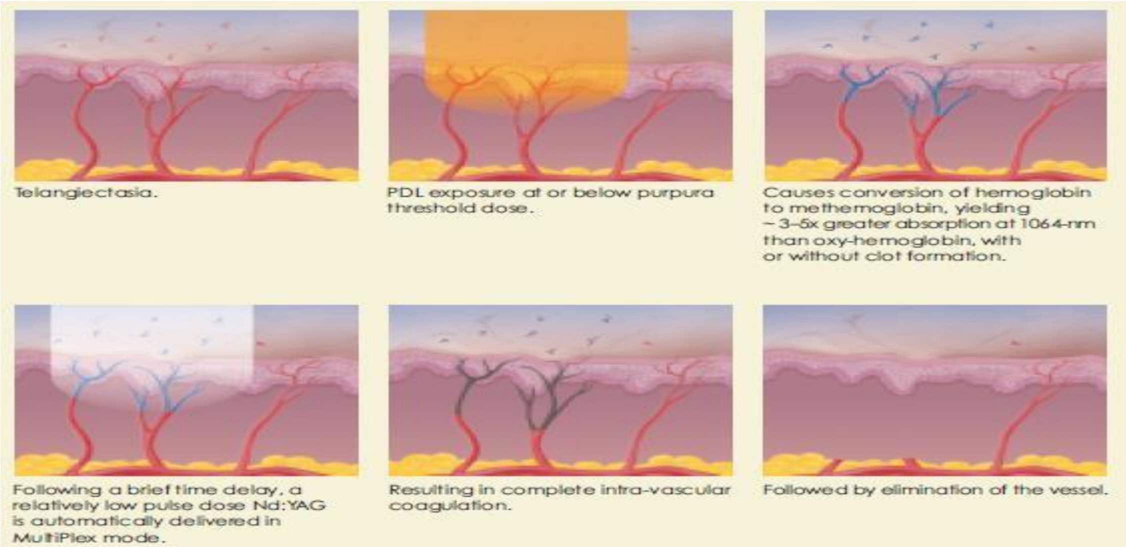

Figure (7): Multiplex Technology.

Treatment Considerations and Experimental Work

• adequate pulse duration with vessel volume. As the vessel volume increase the pulse duration increase.

• Laser spot size is proportional to the volume and depth of the blood vessel.

• Less fluence should be used with purple or blue vessels due to higher light absorption than the red and pink vessels.

• Laser fluence should be adjusted according to vessel type, diameter, depth, and blood pressure.

• Correct diagnosis is essential, particularly in the skin of color.

• A topical anesthetic may be applied in patients who could not tolerate the pain of treatment.

• Pulsed dye laser can accidentally cause hair loss; hair-bearing areas should be covered, e.g., eyebrows and beard.

• The patient and doctor should wear eye goggles throughout the procedure. An optical density of at least 4 (light transmittance 0.01%) is required for a laser goggle that protects against a specific laser wavelength.

• If the treatment is close to the eyelid, a corneal eye shield should be placed (a metallic corneal eye shield provides better protection).

Epidermal Cooling

Pre- and postoperative cooling is of utmost importance to prevent tissue damage and scarring. The epidermal melanocytes and keratinocytes tend to absorb some amount of the high light energy needed to coagulate the deeper vessels; appropriate cooling of the epidermis can protect its temperature from exceeding its threshold for thermal injury. While cooling may minimize epidermal damage, it paradoxically reduces the efficacy of lasers, by blanching the underlying blood vessels.

Patient Selection and Counseling

Patient selection should be done carefully. A thorough examination and evaluation of the patient should be done before enrolling them for treatment. Patients should be counseled in detail about the nature of the lesion, the different treatment options available, and their possible outcomes and complications.

Patients who have any history of photosensitivity disorder, epilepsy, keloidal tendencies, patients on the photosensitive drug, pregnant females, and uncooperative patients with unrealistic expectations should not be enrolled for treatment. Patients with a port-wine stain on the face in the distribution of deep dermatome should be evaluated for possible glaucoma. A magnetic resonance imaging scan of the head and neck should be done in relevant cases. Doppler study of the vascular lesions should be done to rule out arterial and venous ectasia.

The patient must sign an informed consent form. In the case of minors, consent should be obtained from any one of the parents. Photographs of the lesions should be taken during each session to compare the treatment outcome.

Preoperative Anesthesia

Laser treatment causes mild discomfort rather than pain. Most of the patients usually tolerate the discomfort well. Anesthesia may be required in patients who are apprehensive and also in children.

General anesthesia can be considered in children who are having large lesions and those who are very un-cooperative. This is sometimes difficult for dermatologists as it requires a huge setup. Topical anesthesia like EMLA (eutectic mixture of local anesthetics) or local anesthesia like 1% lignocaine is more convenient and is also effective in reducing the discomfort to the patient. In children below the age of 6 months, EMLA should not be used as it may get absorbed and may cause methemoglobinemia leading to cerebral hypoxemia.

Preoperative Care

Broad-spectrum sunscreen should be started 4 weeks before treatment wherever applicable. Preoperative photographs should be taken at the beginning of each session. Treating doctors should wear protective goggles provided by the laser company. Eye shield should be used to protect the patients. Cooling of the skin should be done immediately before starting the treatment.

Postoperative Care

Postoperative epidermal cooling should be done immediately after the laser treatment. Patients should be advised to use topical antibiotic ointment for a few days at the treated site to prevent infections. Patients should continue to use broad- spectrum sunscreen daily wherever applicable. The patients should avoid exercising and swimming during the healing period.

Experimental Work

Two subjects were enrolled for treatment of PWS in two stages, Early and Mature. Treatment of PWS usually takes more than one session, depending on the type and spread of the lesion. In our work, due to the lack of time, we observed one session of each case at Dr. Zeyad Al Rawi & Dr. Mohannad Zeyad Al Rawi Derma Clinic, Al-Harthya- Baghdad/ Iraq. Other sessions were carried out by the doctor. Firstly, the skin is cleaned with soap and warm water, then cleansed with an alcohol rub to ensure that the skin is perfectly clean of facial oils, makeup leftovers, sunblock, or any other substrate that lowers the laser efficiency. Then, the treated area is examined by a dermatologist to specify the required laser parameters for the treatment. A special sunglass was given to the patients to protect their eyes from any reflected laser radiation.

A novel technology (Cynergy, Cynosure, Inc., Westford, MA) that combines 595 nm PDL and 1064 nm Nd: YAG lasers. The Multiplex feature of the Cynergy device delivers sequential, timed pulses from the two laser heads through a single fiber handpiece. The application of 595 nm light followed by the 1064 nm wavelength takes advantage of a chromic shift in blood when heated above 62° C: the oxyhemoglobin absorption coefficient peaks at 595 nm whereas the methemoglobin absorption coefficient aligns with 1064 nm. The combination laser is best used for advanced (darker, thicker, nodular) and/or recalcitrant PWS, whereas the PDL portion of the system can be used alone for superficial/early (pink) PWS, and the Nd: YAG laser can be used alone to provide more effective treatment of PWS in patients with darker skin tones. Treatments were performed in conjunction with cold-air cooling (Zimmer Cryo 6, Cynosure, Inc.). The treatment endpoint was a change in PWS color, disappearance, or inability to blanch and refill. Evaluation of treatment was based on a comparison of pre-treatment and post-treatment photographs.

Results and Discussion

Patient one: Early PWS, 1-year-old boy was born with pink patches on his brow and temple, as seen in figure (3.3-a). PDL treatment was initiated at 4.5 J/cm2 (0.5 ms, 10 mm spot). Five additional PDL treatments were delivered at 2-month intervals (4.5-6 J/cm2, 0.5-6 ms, 10 mm spot) with marked lesional fading. Figure (8.b) shows the PWS immediately after treatment, the skin appeared mildly erythematous and edematous. No purpura, vesiculation, pigmentary abnormalities, or scarring were observed.

A *B*

Figure (8): Early PWS

a: Before, b: After five Treatments in Two Months Interval

Patient Two: Mature PWS, a 34-year-old woman presented with an advanced PWS on the brow and temple. Figure (3.4-a) No prior treatment had been obtained. Multiplex treatment was delivered with sequential 10 mm pulses of the PDL (6-7.5 J/cm2, 6 ms pulse duration) and Nd: YAG (30-35 J/cm2, 10-15 ms) at bi-monthly intervals. Immediately after each treatment, the lesion appeared slightly darker and swollen. No other side effects were noted. Progressive lesional lightening was noted after each of the eight laser treatments as seen in figure (3.4-b).

A

B

Figure (9): Mature PWS

a: Before, b: After Eight Treatments

Treatment was well tolerated by subjects. There were no side effects other than transient discoloration which subsequently resolved spontaneously. All Multiplex laser-treated areas exhibited improvement. Results are presented in the before and after images.

Conclusion

Though Pulsed dye laser is considered the gold standard of vascular lasers; Nd: YAG lasers which are more widely available, have come up as a cost-effective alternative. Thorough knowledge of the patient's condition and understanding of basic laser physics will help the doctor in selecting appropriate pulse duration, spot size, and fluency. However, more quality data is awaited in establishing the efficacy and safety of Nd: YAG laser in various vascular malformations, especially in the context of darker skin types. An optimal cooling system should be used to prevent pain, burning, and dyschromia.

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