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KTP (532 nm) Laser Enhances the Effect of ND:YAG (1064 nm) Laser in the Treatment of Nevus of Ota

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Abstract

Background Nevi of Ota is usually present at birth. It may be congenital but is not hereditary.

Objective To determine the efficacy and side effect profile of Q-switched Nd:YAG and KTP Laser on fourteen patients with nevus of Ota.

Methods Fourteen patients were treated with Q-switched ND: YAG (1064 nm) and KTP (532 nm) laser for a period of 21 months. Six-month follow-up was done after the last session. Response to the treatment was graded on quartile grading scale.

Results Near total improvement was observed (grade IV) in 36% patients, marked improvement (grade III) in 28.5%, moderate improvement (grade II) in 28.5%, and minimal improvement (grade I) in 7% of the patients. Regarding complication (not permanent), no textural change or scaring. When Nd:YAG laser was only used to treat nevi of Ota for three sessions the response was less than 10% improvement in the lesion. When KTP used in combination with Nd-YAG alternatively there was an increasing improvement in most cases up to more than (70%).

Conclusion Concurrent use of the Q-switched 532 in combination with the (1064 nm) Nd:YAG is more effective in pigment clearance than the Q-switch (1064 nm) alone for nevus of Ota.

Keywords Nevus of Ota, Q-switched Nd:YAG (neodymium-doped yttrium aluminum garnet).

List of Abbreviation:

QS = Q-switched, Nd:YAG laser = neodymium-doped yttrium aluminium garnet, KTP laser = Potassium titanyl phosphate, nm = nanometer, ns = nanosecond, mm = millimeter, Hz = Hertz, j/cm= joule/ centimeter, µm = Micrometer

Introduction

Nevus of Ota is also known as nevus fuscoceruleus ophthalmomaxillaris. The lesion may not appear until the ten years [(1)]. It persists throughout life. Eighty percent occur in females; 5% are bilateral [(1)]. This disorder is very common in Asian populations and it has been said to occur in 1% of dermatologic outpatients in Japan, it has been reported in east Indians, among black people and rarely in white population [(2)]. Nevus of Ota may be bilateral; it may be congenital but is not hereditary [(2)]. The entire patient in this study, have no family history.

The cause of Nevus of Ota is not fully known, it is generally believed that nevus of Ota, during early embryonic life, represents a failed migration of melanocytes from the neural crest to the dermo-epidermal junction and subsequent arrest within the dermis [(3)]. Some have hypothesized that sex hormones play a role in its pathogenesis, given the female predominance [(4-6)].

Nevus of Ota typically presents as unilateral blue-black or slate gray macules [7,8], that are located in the distribution of the first or second branches of the trigeminal nerve, tympanic membrane, oral, ear, scalp [9], cornea, iris and retina [9,10]. Nasal mucosal involvement is common [10].

Involvement of hard palate is rare [9,11]. As already stated, most patients tend to develop the nevus at birth or shortly thereafter, although some patients can develop it as late as 20 years of age [10]. Therefore, diagnosis is mainly clinical and a biopsy is rarely needed [10]. The condition is more common in female with male:female ratio 1:4.8 [10, 12]. Most patients have no family history [13].

In many cases the nevus consists of a melanotic nevoid cells [8] which only become pigmented after stimulating by triggering factors; sex hormone [14], infection, trauma, and ultraviolet light exposure. These factors have been reported to trigger the onset of nevus [8,15]. Histologically elongated dendritic melanocytes are scattered widely in the papillary to mid reticular dermis. Hirayama and Suzuki [16] examined the histological findings of 450 cases of nevus of Ota and classified the condition according to the distribution of the dermal melanocytes as follow:

- Superficial (S): dermal melanocytes are located in the superficial layer of the dermis
- Deep (De): dermal melanocytes are located in the deep layer of the dermis
- Diffuse (Di): dermal melanocytes are evenly spread throughout the dermis:

i. Superficial dominant (SD): diffuse distribution of dermal melanocytes, but with greater concentration in the superficial layer
ii. Deep dominant (DD): diffuse distribution of dermal melanocytes, but with greater concentration in the deep layer.

Complications in this nevus occur mainly in ocular involvement including glaucoma [8], uveitis, cataracts, and rarely orbital and cerebral melanomas [17-19]. Other complications may include psychological impact [10]. In this study 90% of the patients have psychological impact; they used camouflage to cover the nevus.

The objectives of this study was to determine the efficacy and side effect profile of Q-switched Nd:YAG and KTP Laser on fourteen patients with nevus of Ota. And to treat difficult cases by laser which cannot be treated with medical and surgical interruption.

Methods

Fourteen patients of nevus of Ota underwent multiple treatments sessions [14] carried at 2-3 week intervals over a period of 1 year and 9 months with a Q-switched Nd:YAG and KTP laser. These patients presented at the outpatient department of Al-Karkh General Hospital, other hospitals in Baghdad and physicians. Two patients had received surgical treatment for their lesions and failure occurred with scar. The study was done in Laser Medical Research Clinics at Laser Institute for Postgraduate Studies, University of Baghdad. The diagnoses were made on clinical appearance in the skin and the eye. Detailed history, clinical examination, and ophthalmoscopy had been performed in all cases. Most patients were in the age group (16-30) years, eleven females and three males. The nevus in nine patients started at (10-12) years old. In five patients was since birth, only three cases had no eye involvement (21%). The area within the orbital rim was not treated. Two patients had bilateral nevus of Ota (14%). Skin types included type III and IV according Fitzpatrick classification; Sun protection with a broad-spectrum sunscreen cream was advised at the start of therapy and continued throughout the duration of treatment. Topical anesthesia with Emla (eutectic mixture of lidocaine and prilocaine), 1 hr with occlusive dressing prior to laser irradiation was applied.

Patient and doctor in the laser room wore appropriate eye protection goggles specific for this type of laser during treatment sessions.

Therapy was initiated with (1064 nm) Q-Switched Nd:YAG Laser with (3 mm) spot size, at 3 Hz frequency and Pules duration (5-10 ns) and fluence (8.98-11.25 J/cm^2).

Regarding (532 nm) Q-Switched KTP Laser with (3 mm) spot size, (3 Hz) frequency pulse duration (5-10 ns) and fluence (3.98-5.31 J/cm^2). The fluence subsequently increased on subsequent sessions based on the therapeutic response and patient tolerability. The end point for treatment was taken as near total improvement or until a maximum of 14 sessions.

Evaluation of results had been made on visual inspection as well as by comparing serial photographs that had been taken before the treatment and after every laser irradiation session. Six-month follow-up was covered after the last session. Response to treatment in terms of clearance of the lesion was graded based on a quartile grading scale as minimal, moderate, marked, and near total as follow:

Grade I: < 25% improvement, minimal improvement

Grade II: 26%-50% improvement, moderate improvement.

Grade III: 51-75% improvement, marked improvement.

Grade IV: Greater than 75% improvement, near total improvement

No Patients had no improvement or worsening of symptoms. A complication such as hyperpigmentation, hypopigmentation, no scarring or textural change was recorded.

Results

Majority of the patients at the end of the treatment reported some improvement (Table 1).

Table 1. Results of treatment of (14 patient) by KTP and Nd:YAG laser

No. of patient	Improvement	Grade	%
5	Near total	IV	> 75
4	Marked	III	51-75
4	Moderate	II	26-50
1	Minimal improvement	I	< 25

Near total improvement (Grade IV) was seen in 36% as in (Fig. 1A-D).

Marked improvement (Grade III) was seen in 28.5% as in (Fig. 2A-C). Moderate improvement (Grade II) was seen in 28.5% as in (Fig. 3A and B) and 7% patients reported less than 25% clearing of the lesion, which was (grade I) minimal improvement as in (Fig. 4). We found a statistical correlation between the number of treatment sessions and the therapeutic outcome. The age and sex of patients did not in any way influence the treatment outcome. Two Patients who had bilateral involvement, one of them had marked response (Grade III) and the other had near total improvement (Grade IV).

The patient, who had recurrence of the pigmentation during the treatment session, gave history of an increase in pigmentation during menstrual cycle, which indicates the relation between nevi of Ota and hormonal cause.

Fig. 1. Prelaser (Left) and postlaser (Right) fourteen sessions with grade IV (near total improvement)

Complications

We can state the following remarks that were observed during the course of treatment and follow up period (Table 2):

1. Pricking sensation during treatment and post-treatment were common, which was resolved within one day after using bepanthine ointment. This sensation always occurred when KTP laser was used.

Fig. 2. Prelaser (Left) and postlaser (Right) fourteen sessions with grade III (marked) improvement.

2. Observed with either wavelength because of the short pulse duration of the Q-switched modes.
3. Transient post-inflammatory hyperpigment-ation was observed in one patient (7%), which was cleared with the use of sunscreens and bleaching agents after one month.
4. Hypopigmentation occurred in two patients (14%) after using KTP laser in high fluence, 5-25 j/cm^2 (Fig 5).

Fig. 3. Prelaser (Left) and postlaser (Right) fourteen sessions with grade II (moderate) improvement

Fig. 4. Prelaser (Left) and Postlaser (Right) fourteen sessions with grade I (minimal) improvement.

Fig. 5. Hypopigmentation after KTP laser in two patients.

5. Recurrence was seen in three patients (21 %).

Some of the complications were noticed and most of them were reversible, as listed in table 2.

Table 2. Some of the complications of laser treatment in patients with nevi of Ota

Complication	No. of patient/ Nd:YAG Laser	No. of patient/ KTP Laser
Pain sensation	-	14
Scarring or texture change	-	-
hyperpigmentation	-	1
Hypopigmentation	-	2
Recurrence	3	3

Discussion

The treatment options for nevus of Ota prior to the advent of laser were limited. These included cryotherapy [(20)], dermoabrasion [(21)], surgical excision [(22)], and cosmetic camouflage. The surgical treatment options were associated with significant scarring and permanent pigment alteration. Q-switched (QS) lasers have changed the management of pigmentary lesions to a great extent. In addition, it is ideal for treating pigmented skin lesions [(28,29,36,41)]. In Ota nevus Melanin absorbs and localizes the high-intensity irradiation from Q-switched lasers, thereby creating a sharp temperature gradient between the melanosome and other surrounding structures. This gradient leads to thermal expansion and the generation and propagation of acoustic waves, which can mechanically damage the melanosome-laden cells. Tissue repair following laser-induced melanosome disruption demonstrates a 2-staged initial transient cutaneous depigmentation followed by subsequent repigmentation weeks later [(23,24)].

According to Polla et al [(23)], and Dover et al [(24)], the destruction of melanosomes is pulse-width-dependent and the longer pulse durations (in microseconds) do not damage the melanosomes. This is consistent with the theory of selective photothermolysis, which states that the pulse duration of an emitted laser wavelength must be less than the thermal relaxation time of the targeted object. Melanosomes are (0.7 µm) in diameter in types I and II skin and (1 µm) or more in diameter in darker skin types. Melanosomes, due to their small size, have very short thermal relaxation times. Q-switched lasers, with pulses in the nanosecond range, provide the most destructive effects on melanosome with the least damage to surrounding cellular structures [(23,24)].

Because of the broad absorption spectrum of melanin (figure 6) [(25,27)], there are numerous lasers that can specifically target pigmented lesions; red-light lasers [e.g., (664 nm) ruby, (755 nm) alexandrite], green-light lasers [e.g., (510 nm) pulsed dye [(26)]. (532 nm) frequency-doubled Nd:YAG], and near-infrared lasers (e.g., (1064 nm) Nd:YAG) [(25)]. It had been found that the Q-switched laser is a treatment of choice for the nevus of Ota [(28)].

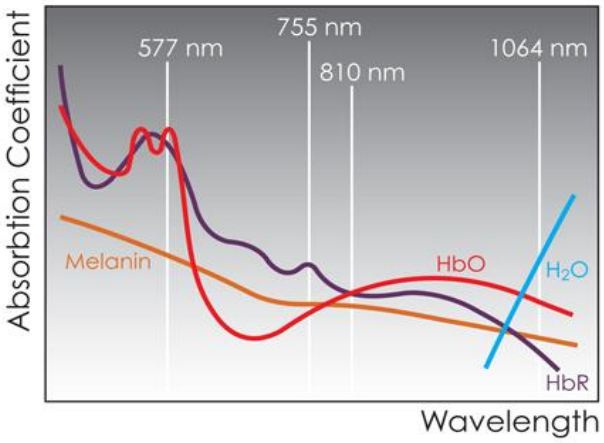

Fig. 6. Absorption characteristics of green and infrared beam Laser [(27)]

In this study, fourteen cases with nevus of Ota were treated, we started first by ND:YAG laser and theclinical improvement in pigment clearance were less than 10%, then we added KTP laser to the treatment alternatively with ND:YAG laser. There was increase in improvement to more than 70% in most cases. We selected both wavelengths (1064 nm, 532 nm) because they fall within the broad absorption spectrum of melanin [(29)].

The result in this study may be explained first, because there is weak absorption by the natural skin chromphores, including melanin at (1064 nm) [30], which may explain the low Incidence of pigmentary changes in nevus of Ota when used (1064 nm) in the treatment only [30]. Second, according to study done by Sherwood et al; the (504 nm) wavelength produced the most pigment-specific injury because the longer wavelengths caused disruption of the basement membrane with pigmentary incontinence [31]. Third, according to Anderson et al study that evaluated the effects of a Q-switched Nd:YAG laser. They show that longer wavelength (which are less well-absorbed by melanin) require a higher energy fluence to induce melanosome changes [32]. Due to these above three reasons, there were less pigmentary changes when we used Nd:YAG (1064 nm) alone at first 3 sessions; but, there was one casethat still had improvement less than 25% after using KTP laser with Nd:YAG. This result may occurr because the (532 nm) laser had epidermal and upper dermal affect (Table 3). Due to its short wavelength the KTP laser cannot reach deep dermal layers [33].

According to the Suzuki histopathology [16], the distribution of the dermal melanocytes in nevus of Ota occurs either in the superficial dermal layer or in the deep dermal layer. So that the lesion with superficial dermal melanocyte improved quickly after four sessions by KTP laser (532 nm), while the lesion with deep dermal layer melanocyte had little improvement after four sessions by KTP laser.

Lastly, according to different studies had done in the laser management of Ota, the use of two wavelengths gave good result in pigment clearance than the use of one wavelength laser radiation [34,36].

In this study; the complication were few and most of them were reversible:

- Transient post-inflammatory hyper-pigmentation, this may be due to possible neglecting the use of sunblock by the patientsafter the laser session.
- Hypopigmentation which may be due to melanocytic damage [33] after using KTP laser in high fluence, (5-25 j/cm^2); because dark-skin patients may also require starting laser sessions at lower energy levels than white-skin patients [40], Hypopigmentation is gone after three months.
- Recurrence may be due to residual melanocytes that have not been targeted or which did not contain sufficient melanin for eradication [37,38].

Table (3): Laser parameters

Parameter	Q-Switched Nd:YAG	Q-Switched KTP
Wavelength	1064 nm	532 nm
Pulse width	5-10 n-sec.	5-10 n-sec.
Fluence	(8.98-11.25) J/cm 2	(3.98-5.31) J/cm 2
Spot size	3 mm	3 mm
Number of pulses/sec.	3 Hz	3 Hz
Number of passes	1	1
Number of laser sessions	10-14	10-14
Pulse overlap	50%	50%
Target chromphores	Melanin, blue-black tattoo pigment	Melanin, hemoglobin
Mechanism of action	Selective photothermolysis	Selective photothermolysis
Absorption/ penetration characteristics	Deep into the dermis	Limited into the epidermis and upper dermis (33)

On the other hand, the recurrence may be due to the presence of deep nests and sheets of nevus cells extending into the reticular dermis or even the subcutaneous fat [39].

Conclusion

Patients of Nevus of Ota were treated with Q-switched (532 and 106 4nm). Concurrent use of the Q-switched (532 nm) in combination with the (1064 nm) Nd:YAG is more effective in pigment clearance than the Q-switch (1064 nm) alone for the treatment of nevus of Ota.

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Author Contribution
The study was done by Dr. Mohammad Ali under the supervision of Prof Dr. Shakur.

Conflict of Interest
Authors declare no conflict of interest.

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