Sudan University of Science and Technology

Collage of Graduate Studies

Utilization of Nd-YAG Laser in Treatment of Onychomycosis in Sudanese Patients

إستخدام ليزر النيوديميوم ياك في علاج فطريات الأظافر لدي المرضي السودانيين

A research project submitted for the requirement of post graduate diploma in laser applications in medicine

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بسم الله الرحمن الرحيم

قال تعالى:

{فَتَعَالَى اللَّهُ الْمَلِكُ الْحَقُّ وَلَا تَعْجَلْ بِالْقُرْآنِ مِنْ قَبْلِ أَنْ يُقْضَى إِلَيْكَ وَحْيُهُ وَقُلْ رَبِّ زِدْنِي عِلْمًا }

صدق الله العظيم

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الإهداء

ببريق الاحترام والتقدير .... لاساتذتي الاجلاء

وبرونق الحب والتبجيل ..... لامي وابي

وبدفئ العشق المستحيل ..... لزوجي وابنائي

وبمبدأ العرفان بالجميل .... لكل من ساعدني

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*Firstly all the praises and thanks be to **Allah.** This work will not be done without the participation of my beloved patients in Khartoum dermatology hospital, so I send to them my gratitude and appreciation.*

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List of abbreviations

DNA	Deoxyribonucleic acids
DLSO	Distal lateral subungual onychomycosis
FDA	Food and drugs administration
KOH	Potassium hydroxide
LPNY	Long pulse Nd-YAG laser
MLSO	Medical laser officer
Nd-YAG	Neodymium – doped yttrium aluminum garnet
PD	Pulse duration
QSNY	Q switch Nd-YAG laser
RNA	Ribonucleic acid
TND	Total nail dystrophy

Abstract

This is a quasi experimental study of the effect of utilization of long pulse Nd-YAG laser in the treatment of onychomycosis. Conducted in Khartoum dermatology hospital- laser unit during the period from May 2018 to August 2018.

The objective of this study was to study the effect of long pulse Nd- YAG laser in the treatment of onychomycosis.

Ten patients were enrolled in the study, with total number of 63 affected nails. All patients were treated with Nd:YAG 1064 nm, fluence was (60-80) J/cm^2, pulse duration 5 ms, spot size 3 mm, 1 Hz frequency and 3 passes. A full course of treatment was consisted of four sessions, with one week interval. Treatment outcome were determined by the assessment of clinical improvement, patient satisfaction and mycological results. The study found that, clinical improvement was achieved among fingernails in 7 patients (77.8%) (p value < 0.05), and among toenails in 2 patients (33.3%) (p value > 0.05). On the other hand, mycological clearance achieved in 8 patients (89.9%) with finger nails involvement (p value < 0.05), and 4 patients (66.7%) with toenails involvement (p value < 0.05). the last criteria for assessment was patient satisfaction, which was achieved in 2 patients (33.3%) with fingernails involvement (p value > 0.05) and only one patient (16.7%) with toenail involvement (p value > 0.05). The final clinical response was determined by using the score of three above mentioned criteria; excellent response was achieved in 2 patients (22.2%) among fingernails and 0 patients (0%) among toenails. Good response was achieved in 5 patients (55.6%) among fingernails and 2 patients (33.3%) among toenails. Poor response was achieved in 2 patients (22.2%) among fingernails and 2 patients (33.3%) among toenails. No response was achieved in 0 patients (0%) among fingernails and 2 patients (33.3%) among toenails.

Finally, Laser is a safe treatment that may be especially useful in patients with contra indication to systemic antifungals like liver diseases. Further large Randomize Control Trails are needed in order to confirm this results.

مستخلص الأطروحه

هذه دراسة شبه تجريبة عشوائية لتحديد مدي فعالية النيوديميوياك في علاج فطريات الأظافر لدي بعض المرضي السودانيين. وقد اجريت الدراسة في مستشفي الخرطوم للامراض الجلديه والتناسلية في الفترة من مايو 2018 الى أغسطس 2018 م.

الهدف من الدراسة هو تحديد مدي فعالية ليزر النيوديميوياك في علاج فطريات الأظافر. تم تحديد استجابة المرضي للعلاج بالإعتماد علي ثلاثة معايير هي: الفحص المخبري، الكشف السريري، و رضاء المرضي عن نتيجة العلاج. اظهر الفحص المخبري ان 7 مرضي (77.8%) من المصابين بفطريات أظافر الأيدي و مريضين (33.3 %) من المصابين بفطريات أظافر الأرجل حصلوا علي نتائج سالبة للفطريات. من جهة أخري بين التقيم السريري ان 8 مرضي (89.9 %) من المصابين بفطريات أظافر الأيدي قد تحسنوا مقارنة ب 4 مرضى (66.7 %) من المصابين بفطريات أظافر الأرجل. وبقياس معدل رضي المرضى عن العلاج، فإن 2 من المرضي (33.3 %) كانو راضين عن نتيجة العلاج في أظافر الأيدي بينما مريض واحد فقط (16.7 %) رضي عن نتيجة العلاج في أظافر الأرجل.

وجدت الدراسة ان العلاج بالليزر خيار آمن لعلاج الفطريات خاصة للمرضى الذين يعانون من أمراض الكبد او الذين لم يستجيبوا للعلاجات الفموية. كما اوصت الدراسة بضروة توعية مرضي فطريات الأظافر بالتغيرات التي تحدث في الاظافر وكيفية العناية. و اقترحت الدراسة أن تجري مزيدا من الدراسات التجربية في هذا المجال للتأكد من صحة النتائج.

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1.1. Introduction

Onychomycosis is a common fungal infection of the nails, which represents up to 50% of all nail problems and 30% of all cases of dermatophytosis (Faergemann and Baran, 2003). It cause characteristic nail changes include; onycolysis, Subungual hyperkeratosis, pitting, thickening and discoloration (Roberts, 1992) (Leelavathi *et al*., 2012). Recently there has been a worldwide increase in the incidence of onychomycosis due to increase in immunocompromised patients, diabetes, use of occlusive footwear's and nail trauma (Malhotra *et al.*, 2016). The common organisms responsible for onychomycosis are *Trichophyton* spp., *Candida* spp. and *Aspergillus* spp. The causative agents may differ from country to country or region to region; in the West, dermatophytes are the commonest causative agents, while in tropical countries, non-dermatophyte moulds and yeasts were found to be common (Leelavathi *et al.*, 2012).

Diagnostic techniques for onychomycosis include specimen analysis by direct microscopy and fungal culture. Other analytic techniques include histologic analysis, immunohistochemistry, flow cytometry, in vivo confocal microscopy, scanning electron microscopy, and polymerase chain reaction (PCR) methods (Gupta and Ricci, 2006).

Many options for treatment of onychomycosis are available; oral therapy, such as Terbinafine, Itraconazole and Griseofulvine are interfering with fungal cell membrane synthesis and causing fungal toxicity. However, treatment with antifungals does pose the risk of potential side effects including gastrointestinal disturbances, skin rashes, pancytopenia, agranulocytosis, liver toxicity, drug interactions and drug resistance (Roberts, *et al*. 2003)(Gupta, *et al*. 2004).

Topical therapies have become increasingly popular because they have none of the adverse effects associated with systemic treatment. Topical therapies include Ciclopirox, Amorolofine, Imidazoles, Tolnaftate, and topical Terbinafine. They have low penetration rate to the nail plate, however, with the introduction of trans-ungual delivery, chemical penetration enhancers, bioadhesive polymers, surface modifiers and ultrasound, their efficacy seems to be improving (Baran and Kaoukhov, 2005). Topical treatments do not perform well when there is multiple nail involvement, or involvement of more than the distal two-thirds of the nail plate or lunula (Abadi and Zderic, 2011). Device-related therapies such as chemical or surgical debridement as well as laser therapies have become increasingly popular in the treatment of onychomycosis (Gupta, *et al*., 2004).

Many researchers believe that laser treatment of onychomycosis is safe and effective with fewer side effects (Bristow, 2014) (Li *et al.*, 2016). Treatment of onychomycosis with Nd:YAG lasers emitting a wavelength of 1064 nm is a relative new treatment modality with promising results. Highly different treatment parameters with pulse durations varying from 0.3ms to 35ms, fluences from 5J/cm^2 to 324J/cm^2, numbers of passes from 1 to 5 and pulse rates from single shot to 5Hz, have been used. Also, the numbers of treatments and treatment intervals is greatly different from study to study (Bjerring *et al*,. 2015).

In Sudan there is no published data regarding the treatment of onychomycosis with Nd - YAG or other types of lasers.

1.2. Literature Review

1.2.1. Background

The literature was identified mainly by extensive searching of various large online databases such as Henari, PubMed, and Medline. Some articles were the result of using search web sites such as Google Scholar. Additional information were collected from text books available at local libraries. Search terms used alone or in combination, included onychomycosis, laser, nails, Nd-YAG.

1.2.2. Nails

1.2.2.1. Developmental anatomy

The nails are originated from the primitive epidermis between the 9th and 20th weeks of intra-uterine life. Complete nail plate reaches the tip of the digit by 36 weeks. It is surrounded by prominent lateral nail folds and a well-developed cuticle (Tony *et al.*, 2004).

1.2.2.2. Nail anatomy

The figure below shows nail anatomy.

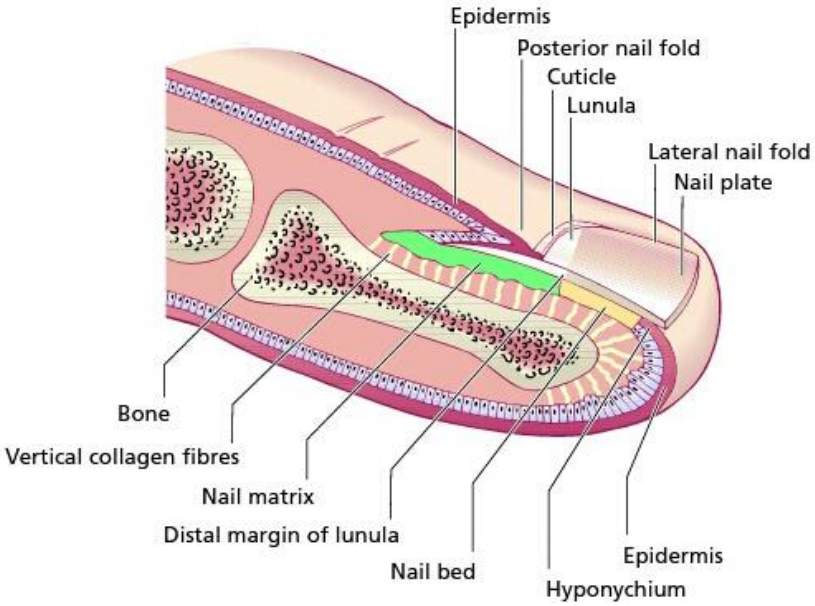


Figure 1.1: Longitudinal section of the digits.

- **Nail matrix:**

It is the main structure of the nail. It produce the nail plate. It is divided into three main parts; dorsal, intermediate and ventral (figure 1.3.1). When the matrix cells

divided it produce new nail plate cells, which emerge as rounded white cells. As the new cells move distally the older nail plate cells become pressed, flat, and semitransparent, so the blood vessels below it become visible giving the pink color of the nail (De Berker, 2013) (Baran, 2015).

- **Nail plate:**

It is rectangular structure, stick on the nail bed, it is consisting of hard keratinized squamous cells (De Berker, 2013).

- **Nail bed**

It is the skin beneath the nail plate, it is composed of epidermis and dermis (Baran, 2015).

- **Proximal nail fold**

Composed of a dorsal roof and a ventral floor. It is 15 mm far from the distal interphalangeal joint (De Berker, 2013).

- **Lateral nail folds**

They are rolls of connective tissue covered with normal epithelium. They have protective function to the nail plate (De Berker, 2013).

- **Lunula**

It is the distal extent of the germinal matrix, it has characteristic white colour and moon shape. It is largest in the thumb and often absent in the little finger (Tony *et al.*, 2004).

- **Hyponychium**

It is the epithelium located beneath the nail plate at the junction between the free edge and the skin of the fingertip (Baran, 2015).

- **Eponychium**

It is small band of epithelium that extends from the posterior nail wall onto the base of the nail. Together, the eponychium and the cuticle form a protective seal. The cuticle on the nail plate is dead cells and is often removed during manicure, but the eponychium is living cells and should not be touched (De Berker, 2013).

- **Nail root**

It is the base of the nail embedded underneath the skin (Baran, 2015).

- **Distal edge**

It is the anterior margin of the nail plate corresponding to the abrasive or cutting edge of the nail (Tony *et al.*, 2004).

- **Paronychium**

It is the border tissue around the nails. Paronychia is an infection in this area (Baran, 2015).

1.2.3. Onychomycosis

1.2.3.1. Definition

"Infection of the nail apparatus by dermatophytes, moulds or yeasts" (Kaur *et al.*, 2008). It is represent about 30% of cutaneous mycotic infections, and 50% of all nail disorders (Faergemann and Baran, 2003).

1.2.3.2. Causative Agents

Onychomycosis is either primary diseases caused by pathogens invading the healthy nail plate, or secondary infection of nails with a preexisting disease e.g. psoriasis (Kaur *et al.*, 2008). Primary onychomycosis mainly caused by dermatophytes, while the non-dermatophytic fungi are responsible for secondary onychomycosis. Dermatophytes are keratophilic fungi, they contain several enzymes, which utilize keratin as source of nutrition (Torres *et al*, 2000). The most frequently isolated species are *Trichophyton rubrum*, *Trichophyton mentagrophytes* and *Epidermatophyton floccosum*. They are responsible for over 70% of all cases (Faergemann and Baran, 2003).

Yeasts are the second cause of onychomycosis. They are responsible for 5.6% of cases. *Candida* species especially *Candida albicans* is the main pathogen (Foster, *et al* , 2004).

Non-dermatophytic fungi are the last cause of onychomycosis. They are uncommon with prevalence rates ranging from 1.45% to 17. 6% (Tosti, *et al,*. 2000). *Scopulariopsis brevicaulis*, is the most common isolated mold. Mixed infection with more than one pathogens has been reported as high as 17.6% (Tosti, *et al,*. 2000). some studies reported that, In tropical area non dermatophytic fungi are more common than dermatophytes (Leelavathi *et al*, 2012) (Shahzad *et al.*, 2014)

1.2.3.3. Clinical features

There are five clinical presentations of dermatophytic onychomycosis (Tony *et al*, 2004):

1. **Distal and lateral subungual onychomycosis (DLSO)**

It is the most common pattern of infection, starting from the hyponychium. The fungus affects the nail bed and the nail plate up to the lateral margins of the nail. The

infection can gradually reach the matrix. As the disease progresses, the nail plate undergoes clinical changes such as thickening, onycholysis and a yellowish discoloration. Occasionally the nail may become darker brown or black. This type is commonly caused by *Trichophyton Rubrum* (Kaur *et al.*, 2008)

2. Superficial white onychomycosis (SWO):

Is a less common type in which the fungus directly targets the upper layers of the nail plate and produces well circumscribed powdery white patches, often away from the hyponychium. It is more common with *T. mentagrophytes* var. interdigitale (Effendy *et al.*, 2005).

3. Proximal subungual onychomycosis (PSO)**:**

It is a rare type, recently it become particularly associated with AIDS patients. Rapid invasion of the nail plate by *Trichophyton rubrum* from the posterior nail fold may develop to produce Yellow or white patches appear around the nail lunula with only marginal increase in thickness (Tony *et al*, 2004).

4. Endonyx onychomycosis:

This is seen with infection caused by dermatophytes that cause endothrix scalp infections. It lead to nail scarring and lamellar splits. The invasion occurs from the top surface, then penetrates deeply into the nail plate. Mainly caused by by *Trichophyton soudanense* (Kaur *et al.*, 2008)

5. Total dystrophic onychomycosis (TDO):

This type cause severe destruction of the nail plate and nail matrix. It may be primary or secondary (Faergemann and Baran, 2003).

Candida onychomycosis usually associated with onycholysis, paronychia and candida granuloma. Some patients may presented with complete destruction of the nail plate. In addition to these conditions, *Candida albicans* invasion may associated with erosion of the distal and lateral nail plate (Kaur *et al.*, 2008).

1.2.3.4. Treatment of Onychomycosis:

Treatment options available are topical antifungals, oral antifungals and surgical removal of the nail plate (Gupta, *et al* 2004). Topical antifungals were rarely used, because nail keratin is both compact and hard, and partially impermeable, thus restricting drug penetration to the organisms causing onychomycosis. The effectiveness of topical treatments can be enhanced when applied as a nail lacquer; Amorolfine and Ciclopirox (Baran and Kaoukhov, 2005). On the other hand oral antifungals are found to be extremely effective, but they carry the risk of hepatotoxicity (Gupta, *et al* 2004).

Surgical removal is an invasive procedure however, secondary bacterial infection is one of the complications. Furthermore, there is a reported 10% to 53% recurrence or relapse rate (Gupta *et al*, 2004). Recently Laser therapy appears as non-invasive and non-hepatotoxic treatment of onychomycosis. Thus many studies have been conducted to assess the efficacy of laser in treatment of onychomycosis and results vary slightly on type of laser and duration of treatment. However, regardless of the treatment, most of the studies are showing positive nail clearance and negative fungal cultures, after treatment with laser (Heath, 2015).

1.2.4. Laser

1.2.4.1. History

The first theoretical foundation of LASER and MASER was given by Einstein in 1917. Maiman's first laser was based on optical pumping of synthetic ruby crystal using a flash lamp that generated pulsed red laser radiation at 694 nm. Iranian scientists Javan and Bennett made the first gas laser using a mixture of He and Ne gases in the ratio of 1:10 in the 1960. R. N. Hall demonstrated the first diode laser made of gallium arsenide (GaAs) in 1962, which emitted radiation at 850 nm. Later in the same year Nick Holonyak developed the first semiconductor visible-light-emitting laser (Fujiro and Yoshinori, 1976).

1.2.4.2. Definition of laser

LASER stand for "Light Amplification by Stimulated Emission of Radiation" (Svelto, 2010)

1.2.4.3. Properties of laser

Laser light has several unique characteristics not shown by light obtained from other conventional light sources, which make them suitable for wide range of applications.

1. **Monochromaticity**

It is the ability of laser to produce single well defined color or wavelength. The wave length emitted by the laser depends both on lasing material and the design of laser cavity (Silfvast, 2011).

2. **Directionality**

It is the property of laser light which allows it to stay tight bound confined beam for a large distance with very little divergence (Silfvast, 2011).

3. **Coherence**

Is the degree of correlation between the phase at two different points on beam of light; all photons are emitted from the laser are in the same phase (Silfvast, 2011).

4. **High intensity**:

Laser light is the intense light ever be known. Intensity can be defined as the number of photons emitted per unit surface area per unit solid angle. Even lasers with low intensity, compared with other lasers, are intense more than the sun light. This property is due to huge number of coherent photons emitted with very small angle (Silfvast, 2011).

1.2.4.4. Construction of laser system:

Certainly, every laser system has an optical cavity consist of active gain medium, placed between two of highly reflecting mirrors with one of them partially transmitting and the other one is totally reflective. In addition, there is a pumping source to raise the atom in to the exited state. The gain media may be solid, liquid, gas or semiconductor. It has the property to amplify the amplitude of the light wave passing through it by stimulated emission (Jawad, *et al.*, 2011). The figure below shows the construction of laser system.

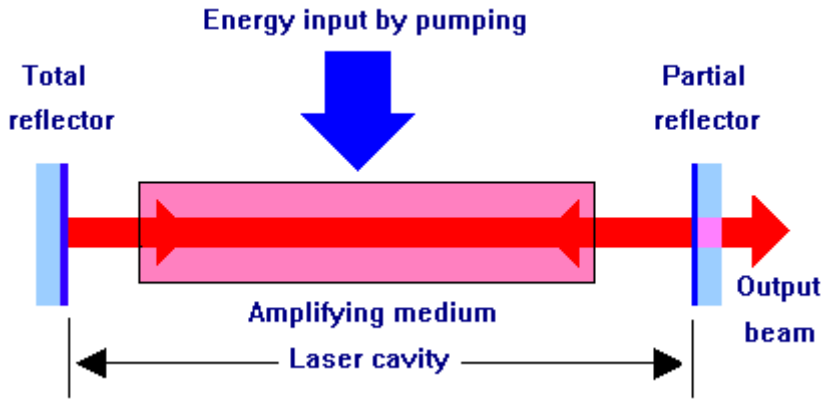


Figure 1.2: Construction of laser system.

1.2.4.5. Principal of Lasing Action:

Lasing action involve four main basic steps including photon absorption, population inversion, spontaneous emission and stimulated emission**.** When energy is applied to a medium, the atoms will absorb energy, become exited to jump to higher energy level from the ground state, this called absorption. As more atoms absorb light, the population in the upper laser level become more than that of the lower level, this is called population inversion. Then the atom will returns to its initial ground state after

staying in that level for a very short duration, emitting a photon in the process called spontaneous emission; a process usually occurs in the conventional light sources (Fujiro and Yoshinori, 1976). When the atom is induced to give up its photon earlier than it would have done ordinarily under spontaneous emission, then tow photons are released from the same excited state in the same phase. This process called stimulated emission; it is essential for laser action. When favorable conditions are created for the stimulated emission, more atoms are forced to give up photons. The highly reflective mirror and partially reflective mirror continue the reaction by directing photons back through the medium along the long axis of the laser cavity. This results in rapid buildup of energy of emitting one particular wavelength (monochromatic light), traveling coherently in a precise, fixed direction. This process is called amplification by stimulated emission. The partially reflective mirror allows the transmission of laser beam when the gain reach the threshold condition (Tarasov, 1986).

1.2.4.6. Classification of Lasers

Lasers are classified in different ways; (Silfvast, 2011)(Singh *et al.*, 2012)

- According to the output power, they are classified into high power and low power lasers.
- According to mode of operation, they are classified in to continuous wave operation lasers (has a constant power output during whole operation time) and Pulsed lasers (emits light in strong bursts periodically with no light between pulses).
- According to the pumping mechanisms, they are classified in to electrical, optical thermal and chemical pumping.
- According to the type of gain medium they are classified in to:

a. Gas Laser

Gas lasers are widely available in almost all power (milliwatts to megawatts) and wide range of wavelengths (UV-IR) and can be operated in pulsed or continuous modes. Based on the nature of active media, there are three types of gas lasers; atomic like He- Ne laser, ionic like Argon ion, and molecular like co_2. Most of the gas lasers are pumped by electrical discharge. Gas lasers are used in applications that require laser light with very high beam quality and long coherence lengths (Silfvast, 2011)

b. Liquid or dye lasers:

Liquids are more homogeneous as compared to solids and have larger density of active atoms as compared to the gasses. They are pumped via flash lap or other lasers. Organic dyes such rhodamine, styryl, coumarin, and stilbene, dissolved in appropriate solvents act as gain media. The broader fluorescence band in dye lasers give them the unique feature of wavelength tuning, so they becoming increasingly important in spectroscopy, holography, and in biomedical applications (Svelto, 2010)

c. Semiconductor Laser

Unlike other types of lasers, semiconductor lasers are smallest, cheapest and are easily scalable. Their conductivity lies between conductor and insulator. The gain medium is made from semiconductor crystal such as gallium arsenide or lead selenide. There are two types of semiconductors, n-type and p-type (Silfvast, 2011)

d. **Solid state lasers**

Solid state lasers are another important family of lasers. The host material consist of crystal of glass like material doped with Chromium, Neodymium, Sapphire…etc. they are usually pumped with flash lamp or laser diode. Ruby, neodymium and Alexandrite are the most famous examples (Tarasov, 1986).

Neodymium is a rare earth material. It provides the laser activity in the crystal. The trivalent ion Nd^{3+} is doped in to the host material YAG (yttrium, aluminium, garnet). Nd:YAG laser has a wave length of 1064 nm and has the capability to reach deeper layers of skin tissue than other types of lasers. It consist of laser rod which is typically 10 cm in length and 12cm in diameter is housed at one foci of the elliptical resonator while a linear flash lap is placed in the other foci. Optical resonators are tow spherical mirrors to compensate lensing effect (figure1.4.3). The pumping mechanism is done by xenon flash lamp. The exited Nd^{+3} ions decay non radiative quickly to the intermediate upper metastable state releasing their excess energy to the crystal. The Nd:YAG system can be used in pulsed or cw mode (Silfvast, 2011) (Fujiro and Yoshinori, 1976). QSNY laser produces two wavelengths, one in the infrared range (1064 nm) and a second beam of 532 nm wavelength which is useful for superficial skin lesions. Nd:YAG laser has been used to treat various skin conditions such as vascular lesions, pigmented lesion and Onychomycosis. It is also used for hair removal and tattoo removal. Several laser devices have been granted FDA marketing approval for the treatment of onychomycosis (Ogden, 2016). The first two lasers that were approved by the FDA for the treatment of onychomycosis are PinPointe FootLaser [Cynosure, Massachusetts, USA] and Cutera GenesisPlus [Cutera, California, USA]) are both

flashlamp pumped short-pulse Nd:YAG 1064 nm lasers. These lasers emit (100–3000) microsecond pulses with an energy fluence of 25.5 J/cm^2 for a 1 mm spot size (Kim *et al.*, 2016). The figure below shows the construction of ND-YAG laser.

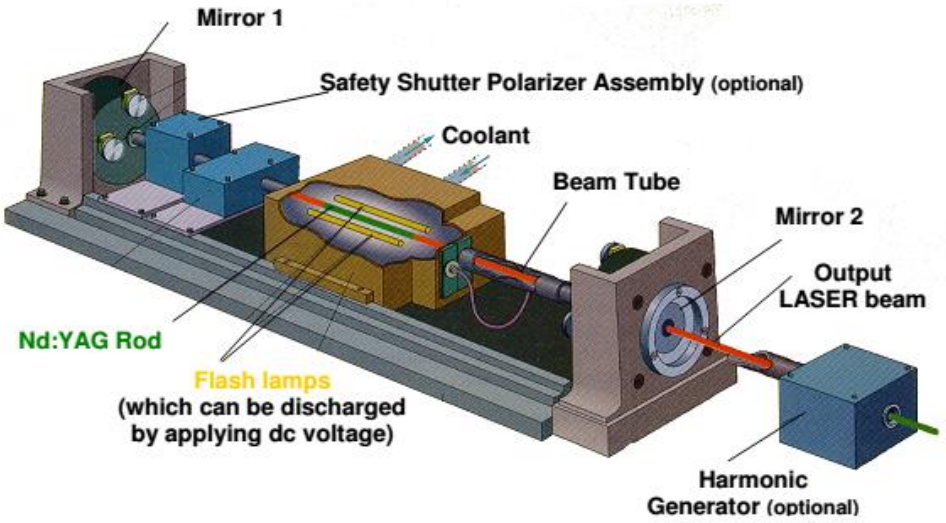


Figure 1.3 Construction of Nd- YAG laser.

1.2.4.7. Laser tissue interaction:

1.2.4.7.1. Optical properties of the tissues:

When light touch the skin a small fraction of light is reflected, but most of laser light penetrates into tissue, where it is either absorbed or scattered by the molecules. Also some of the light may transmit through the layers(Ansari and Mohajerani, 2011)

- **Absorption:**

Absorption of the light by tissues is important for laser to do it is action. Absorbing molecular components of the tissue are called chromophores; porphyrin, haemoglobin, melanin, protein, flavin, retinol and water. Water has two regions of strong absorption, one in UV and one in the IR region. The absorption peak of proteins and nuclide acids is in the UV region between 260 and 280 nm. Blood absorbs light in a broad wavelength region up to red light (630 nm), Melanin absorbs light in a region from UV to near IR (Ansari and Mohajerani, 2011). The figure below shows the chromophore absorption in the electromagnetic spectrum.

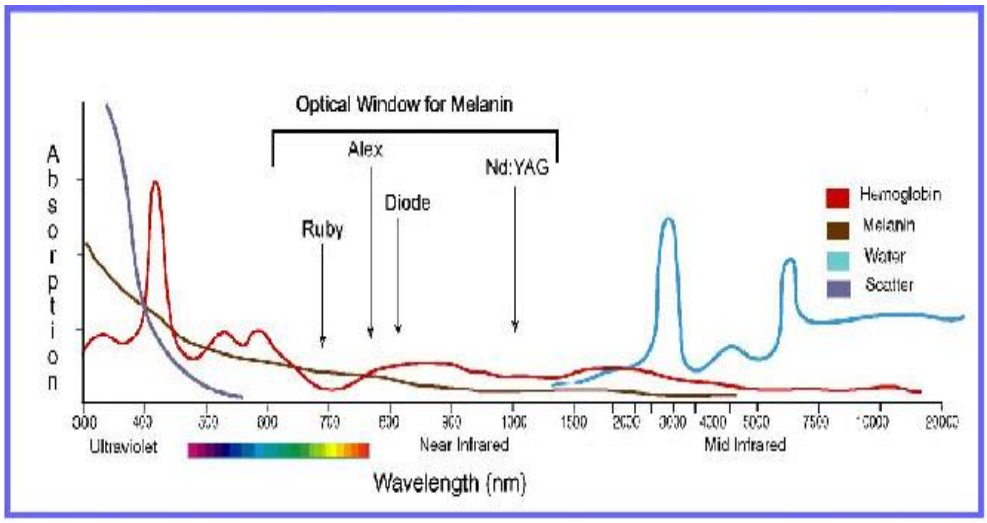


Figure 1.4 Absorption of chromophore by different wave lengths on electromagnetic spectrum.

- **Scattering:**

The scattering behavior of biological tissue is also important, because it determines the volume distribution of light intensity in the tissue.

Scattering is depend on the wave length, shorter wavelengths are scattered more than the longer wavelengths (Ansari and Mohajerani, 2011).

1.2.4.7.2. Laser parameters:

Selective photothermolysis means using light to selectively heat an object to destruct it, while preserving surrounding tissues (Murphy and Torstensson, 2014). Selective photothermolysis requiring right combination of all of the following parameters to achieve the desired effect (LeVeque *et al* , 2003)(Jawa *et al.*, 2011):

- **Wave length**

It is the distance between two wave crest in successive waves in the laser beam. Wavelength affects strength of absorption by skin “chromophores” such as hemoglobin, melanin and water. Longer wavelength has greater penetration than the shorter wave length.

- **Power and energy**

Power density is the quotient of incident laser power on a unit surface area, expressed as watt/cm^2. While the energy fluence is the amount of laser energy delivered in a single pulse and is expressed in j/cm^2.

- **Spot size**

It is the laser beam diameter (in mm) where the laser beam meets the skin. Smaller spot sizes reduce penetration at a given wavelength, due to increase scattering.

- **Pulse duration**

It is the time during which the laser actually emits energy. A pulse duration just shorter than the thermal relaxation time (TRT) of the target substance will allow selective heating of the target, limiting thermal damage to surrounding tissues. The TRT was defined as the time taken for the temperature of the heated target to decrease by 50%. Most selective thermal damage occurs when light energy is delivered to the target tissue faster than the rate at which the target tissue can cool down (Murphy and Torstensson, 2014).

1.2.4.7.3. The physical mechanism of interaction

- **photochemical reactions**

In low-dose irradiation of living tissue, photons may have an influence on the proliferation of cells. Molecular targets can be cytochrome C oxidase or photoactive porphyrins. Cellular targets are mitochondria with the effects of increased adenosine triphosphate production, modulation of reactive oxygen species, and initiation of cellular signaling. Which lead to increased healing of chronic wounds, nerve injury and pain reduction (Jawad, *et al.*, 2011).

- **Thermal reactions**

All the surgical applications of lasers, whether in cutting or in hemostasis, rely on the conversion of electromagnetic energy into heat. The energy of laser irradiation is transferred into heat due to absorption of photons by tissue components; DNA/RNA, chromophores, proteins, enzymes, and water. According to the degree of heating, selective thermal damage can be achieved (Ansari *et al*, 2013).

- 42–45° C: beginning of hyperthermia, conformational changes, and shrinkage of collagen;
- 50° C: reduction of enzymatic activity.
- 60° C: denaturation of proteins, coagulation of the collagens, membrane permeabilisation.
- 100° C: tissue drying and formation of vacuoles.
- >100° C: beginning of vaporization and tissue carbonization.
- 300–1000° C: thermoablation of tissue, photoablation and disruption.

- **Electro-mechanical reactions**

At even higher laser energy density, shock waves and other mechanical side effects become more significant. Shock waves, cavitation bubble, jet formation lead to mechanical damage to adjacent tissue (Jawad *et al.*, 2011)

- **Interaction of Nd-YAG laser with nails and fungal elements:**

Although the mechanism of laser treatment of infected nail by fungi is not well known, there are several theories. The Melanin is an essential constituent of the fungal cell wall that has been described in many pathogenic species. The 1064 nm radiation emitted by the Nd:YAG laser is primarily absorbed by dark pigments of the fungi (Kozarev J and Vižintin, 2010). Desired average tissue temperature for laser irradiation of onychomycotic nails is about 43-51^{o}C, at a treatment time of at least 2-3 minutes provides a therapeutic dose. Such increases in local temperature may acts by a regulatory effect on immune function of the tissue, induce apoptosis and rupture of fungal cells membranes (Kozarev J and Vižintin, 2010). The energy produced by by Nd:YAG lasers is absorbed in the region between the nail plate and the nail bed based on the principle of selective photothermolysis where the temperature is increased to thermally deactivate the unwanted organism without causing unwanted injury to surrounding tissue (Wanitphakdeedecha *et al.,* 2015). QSNY laser is expected to have an effect based on specific target-action over the fungus by the absorption of 1,064nm into the melanin of the fungal cell wall and the absorption of 532 nm into the xanthomegnin of *Trichophyton rubrum* (Kim *et al.,* 2016).

1.2.5. Laser safety:

1.2.5.1. Classification of laser hazards (Sliney, 1995)

- **Class I**: Cannot emit laser radiation at known hazard levels.
- **Class II:** They are low power lasers. Their wave length with in the visible light (400-760) nm. Emit laser in either continuous wave or pulsed mode. Radiant power above Class I levels but not more than 1 mW. This class is hazardous only if you stare directly into the beam for a long time.
- **Class IIIA**: They are intermediate power lasers (1-5) mW. They are hazardous for beam viewing, but can be considered safe for momentary viewing except by focusing or directing optics.
- **Class IIIB**: Their power between (5-500) mW, generally they are not capable of producing a hazardous diffuse reflection. It is potentially hazards to the eye even if momentary viewing.
- **Class IV**: They have high power 500 mW or more, they are hazardous to view under any condition (directly or diffusely scattered). They have potential fire hazard and a skin hazard. Significant controls are required for this class.

1.2.5.2. **Hazards of laser** (Barat, 2002)

- Non beam hazards include electric Shock, fire, laser generated air contaminant, chemical hazards, collateral and plasma radiation, noise.
- Beam hazards include both eye and skin hazards; which are shown in the table below.

Table 1.1. Laser beam hazards according to the wave lengths.

Wave length	Eye effects	Skin effects
Ultraviolet C ((200-280) nm)	Photokeratitis	Erythema (sunburn) Skin Cancer
Ultraviolet B ((280-315) nm)	Photokeratitis	Accelerated skin aging Increased pigmentation
Ultraviolet A ((315-400) mm)	Photochemical Cataract	Pigment darkening Skin burn
Visible ((400-780) nm)	Photochemical and thermal Retinal injury	Photosensitive reactions Skin burn
Infrared A ((780-1400) nm)	Cataract, retinal burns	Skin burn
Infrared B ((1400-3000) nm)	Corneal burn Aqueous flare IR cataract	Skin burn
Infrared C ((3000-10000) nm)	Corneal burn only	Skin burn

1.2.5.3. Protection against laser hazards

- A written Laser Safety Policy Program
- Posting of warning signs
- Designation of the authority and responsibility for the evaluation and control of laser hazards to a MLSO.
- Management of incidents (near accidents) and accidents including reporting, investigation, analysis and remedial action
- Training and education of personnel involved in the use and maintenance of lasers; use of safety goggles, closes….
- Formation of a Medical Laser Safety Committee.
- The establishment of a Quality Assurance Program including
- Regular inspection of the laser equipment.
- Presence of another person during maintenance work to provide first aid and to call for assistance in case of an injury or accident.

1.3. Justification

Onychomycosis is rarely life threatening, however, its high incidence and the associated morbidity makes it an important public health problem. Treatment with antifungal therapy remain unsatisfactory because of potential systemic effects of oral therapy and poor penetration of topical medications to the nails. Although Laser therapy is expensive, it has the potential to treat onychomycosis locally without adverse systemic effects; many studies were done worldwide have even reported achieving clinical and mycological cure. To answer the question is Nd - YAG laser is an effective treatment option for onychomycosis in Sudanese patients we need to do this study.

1.4. Objectives

1.4.1. General objective:

To study the effect of utilization of Nd-YAG laser in the treatment of onychomycosis.

1.4.2. Specific objective:

- To assess the response of patients with onychomycosis to Nd- YAG laser.
- To determine any post treatment complications after the treatment of onychomycosis with Nd-YAG laser.

2.1. Study design

Quasi Experimental Trial

2.2. Study area

Khartoum dermatology hospital

2.3. Study population

The study population includes patient with onychomycosis presented to dermatology clinic according to the following criteria.

2.3.1. Inclusion criteria

Any patient 18 years or more, had been diagnosed as onychomycosis clinically and by direct microscopic examination was included in the study.

2.3.2. Exclusion criteria

Any patient receives systemic or topical antifungal in the last year, any patient with any other nail diseases such as psoriasis or lichen planus, any patient with diabetes or malignancy, pregnancy and history of keloid or hypertrophic scar.

2.4. Study duration

From May 2018 to August 2018

2.5. Sample size

Ten patients was selected according to the inclusion and exclusion criteria.

2.6. Data collection

The data was collected using study patient record which include:

2.6.1. Structured interview

After obtaining informed consent, information about each patient was collected including demographic data, past medical history.

2.6.2. Clinical examination

Detailed clinical examination of the nails was done before the laser session to determine nail changes and type of onychomycosis. Examination was done before and after each laser session to determine the clinical improvement and side effects.

2.6.3. Photographs

Photos were taken before each session.

2.7. Laboratory investigations

All patients were evaluated for onychomycosis before and after treatment. Samples was collected with a sterile nail clipper after disinfecting the nail with 70% alcohol. The nail

samples were transported in a pouch made out of paper to microbiology lab. All specimens were subjected to direct microscopic examination. The tests were repeated after the fourth session of laser therapy.

2.7.1. KOH preparation

The specimens were mounted on a clean slide in two drops of 20% potassium hydroxide (KOH) and gently passed over Bunsen burner for a few seconds to accelerate the dissolve of keratin in the specimen. The slides were covered with cover slip and leaved in petri dishes contained wet cotton for 2 hours, and then examined under low and high power magnification for the presence of spores or hyphae.

2.7.2.Methylene Blue

Another specimen also were mounted in a clean slide in one or two drops of normal saline leaved until dried, then it gently passed over Bunsen burner for fixation, then staining with methylene blue for two minutes followed by washing, then seen under the microscope for the presence of pseudohyphae and budding yeast.

Diagnosis of onychomycosis was made by the presence of hyphae, pseudohyphea, or spores on direct microscopic examination.

2.8. Treatment procedure

2.8.1.Treatment machine

Laser treatment was performed using (Cynosures Apogee Elite laser machine, manufactured in USA) which contains two laser systems (Figure 2.1): A 755 nm Alexandrite laser and a high powered 1064 nm Nd:YAG laser with the following characteristics; wavelength are 755 nm and 1064 nm, Laser type Nd- YAG & Alexandrite. Height 41 inch. Length 25 inch. Weight 180 lbs. Width15 inch. Cooling System Cold Air or Integrated Cooling. Pulse Width – 755 nm: adjustable (0.5 – 300) ms & 1064 nm: adjustable (0.4 – 300). Repetition Rate 755: 2Hz & 1064 nm: 5Hz. Spot size Adjustable: (3,5,10,12) mm.

Figure 2.1. Cynosure laser machine & Cynosure air cooling.

2.8.2.Treatment protocol

Before starting treatment, all patients were informed about the laser treatment, potential side-effects and therapeutic alternatives. Then they gave their written consent. All patients were treated with Nd:YAG 1064-nm, fluence was (60-80) J/cm^2, pulse duration 5 ms, spot size 3 mm, and 1 Hz frequency. The entire nail plate were covered with 3 passes of laser (figure 2.2). A full course of treatment was consisted of four sessions which were repeated every week for one month. Cooling with cold air, provided by commercially available air cooling device was used to reduce discomfort.

Figure 2.2. Treatment procedure

2.8.3. Safety measures during treatment

The LPNS emits 1064 nm wavelength, is classified as class IV laser that may cause both optical and cutaneous damage through direct laser beam or reflection. Other non-beam hazards may be encountered. The safety precautions followed in this study were including:

- The safety features of the cynosure Nd-YAG laser system including the locked switches.
- Laser room precautions like warning signs and avoidance of reflective objects like mirrors inside the room.
- Optical hazards precautions like wearing of appropriate goggles by doctors and patients.

2.9. Evaluation criteria

The study used three criteria to determine the efficacy of the treatment. Then any criteria given a score of 1. The final response of the patients were determined by their score; score 3 equal excellent response, score 2 equal good response, score 1 equal average response, score 0 equal no response. The three criteria were as follows:

2.9.1. Laboratory evaluation

Direct microscopic examination was performed after the fourth session of treatment. Then the percent of negative results were calculated.

2.9.2.Clinical evaluation:

All affected nails were examined after the end of four session to determine the clinical improvement. Four clinical signs where used for evaluation; onycholysis, Subungual hyperkeratosis, size and color of the lesion. Each of this signs given 25% of the total score (100%). Improvement of 50% or more considered as improved. Less than 50% considered as not improved. Then the total percent of clinical improvement was calculated.

2.9.3.Patient satisfaction:

Efficacy also was evaluated based on a subjective measure of patient satisfaction. Patients are asked if they are satisfied or not, then the present of satisfied patients were calculated.

2.9.4. Final response:

- Final clinical response was assessed by the calculation of the score of each patient.

- Score 3 (excellent response) was given to patients fulfil all the three evaluation criteria.
- Score 2 (good response) was given to patients fulfil tow of the evaluation criteria.
- Score 1(poor response) was given to patients fulfil one of the evaluation criteria.
- Finally score 0 (no response) was given to patients failed to fulfil the three evaluation criteria.

2.10. Study variables:

- Dependent variable: Onychomycosis
- Independent variable: Age, gender, patient complain, ND-YAG laser, types of onychomycosis, direct microscopic examination, clinical improvement, patient satisfaction.

2.11. Ethical considerations

- The proposal was approved by research committee of institute of laser.
- The study was carefully explained to the participants and written consent was obtained.

2.12. Data analysis:

The data were analyzed using SPSS version 25.

This study was conducted in Khartoum Dermatology Teaching Hospital, in a period from May to August 2018. Ten patients were diagnosed clinically and microbiologically as onychomycosis were included in the study. A total of 63 nails (45 finger nail and 18 toe nail) were treated with Nd-YAG laser 1064nm. . Nine (90%) patients received four sessions while one (10%) patient received 3 sessions of treatment. The results were represented in the form of figures from (2.1 to 2.8) and tables from (2.1 to 2.13).

3.1. Demographic data of patients

3.1.1. Gender of the patients

They were 8 females (80%) and 2 males (20%) involved in the study.

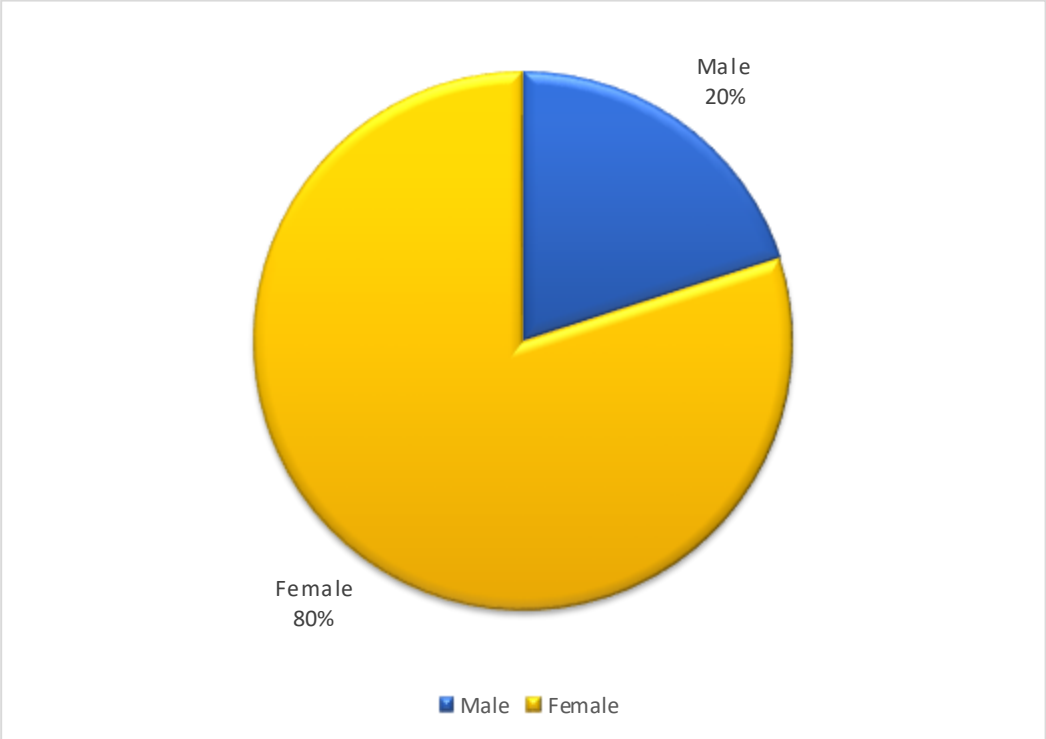


Figure: 3.1 Distribution of patients with onychomycosis according to gender.

3.1.2. Age of the patients

Seven age groups were included in the study; 2 patients (20%) with in the age group between (21-25) years, 3 patients (30%) with in the age group between (26-30) years and 1 patient (10%) in each other age groups.

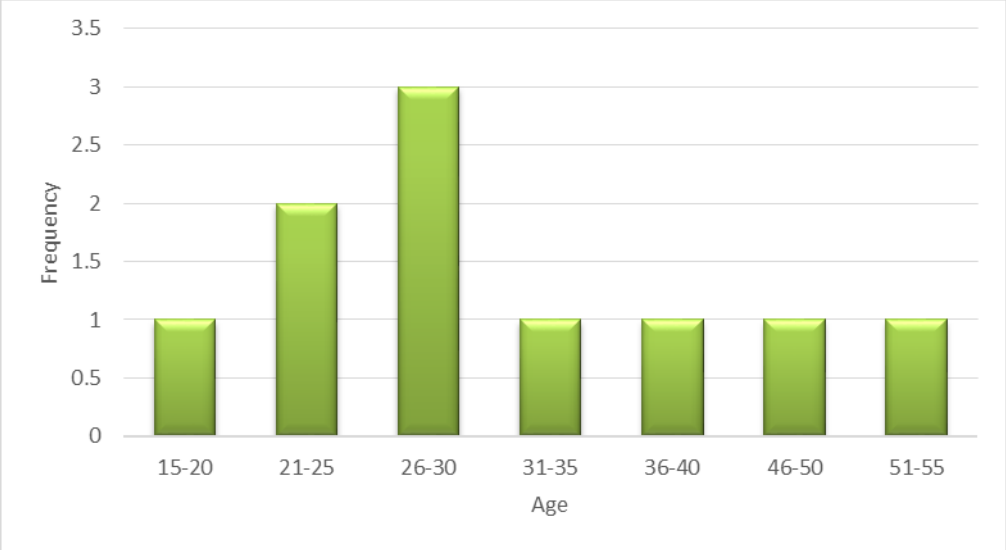


Figure 3.2 Distribution of patients with onychomycosis according to Age.

3.2. Clinical data of patients

3.2.1. Duration of onychomycosis

In this study (3) patients 30% had onychomycosis for 1-3 years, 4 patients (40%) for 4-6 years and 3 patients (30%) had onychomycosis for 7-9 years.

Table 3.1 Distributions of patients according to the duration of onychomycosis.

Duration of onychomycosis		Frequency	Percent
	1-3 years	3	30.0 %
	4-6 years	4	40.0 %
	7-9 years	3	30.0 %
	Total	10	100.0 %

3.2.2. Family history

Two patients (20%) of the patients had family history and 8 patients (80%) had no family history of onychomycosis.

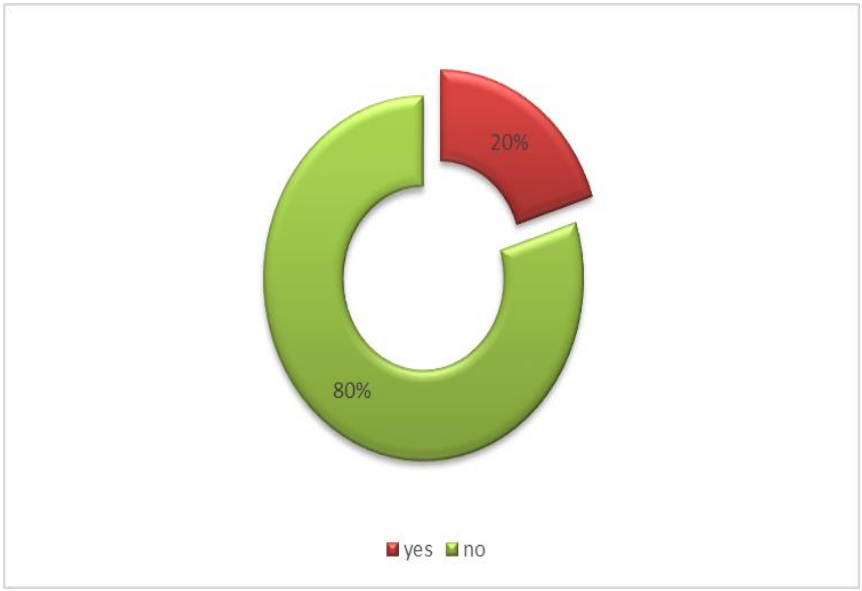


Figure 3.3 Distribution of patients according to the family history of onychomycosis.

3.2.3. Patients complaints

A 5 patients (50%) were complaining of disfigurement while 2 patients (20%) complaining of pain and one patient (10%) complaining of bad odor. The last 2 patients (20%) had no complaint.

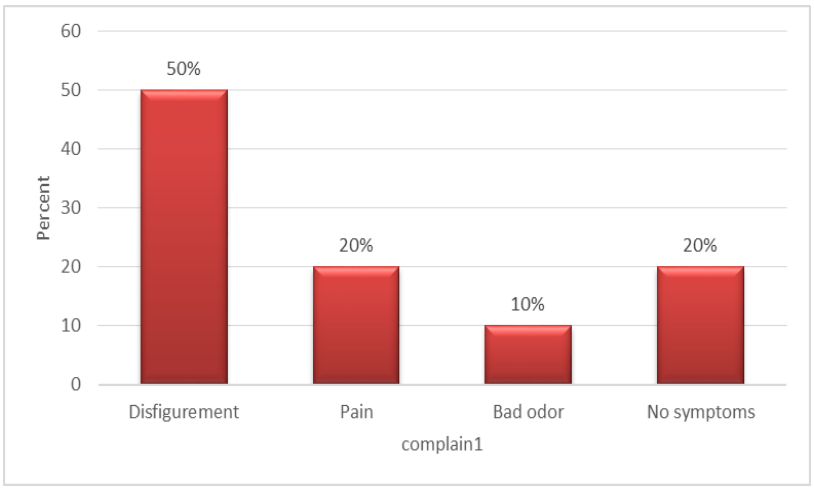


Figure 3.4 Distribution of patients with onychomycosis according to the complaint.

3.2.4. Fingernails and toenails involvement

Four patients (40%) had only fingernails involvement, one patient (10%) had only toenails involvement and five patients (50%) had both toenails and figure nails involvement.

Table 3.2 Distributions of patients with onychomycosis according to the finger nail and toe nail involvement.

Nails	Frequency	Percent
Only finger nail	4	40.0 %
Only toe nails	1	10.0 %
Both toe and finger nails	5	50.0 %
Total	10	100.0

3.2.5. Types of onychomycosis

- The most common type of onychomycosis was DLSO; it was found in 8 patients (88.9%) with fingernails involvement and 5 patients (88.3%) with toenails involvement. while TDO presented only in one patient (11.1%) with fingernails involvement and also one patient (16.6%) with toenails involvement. This agreed with Kozarev and Vižintin (Kozarev and Vižintin, 2010) and Moon (Moon *et al.*, 2014).

Table 3.3 Distributions of patient with onychomycosis according to the type of the disease among fingernails and toenails

Type of onychomycosis	Fingernails	Percent	Toenails	Percent
DLSO	8	88.9 %	5	83.3 %
TDO	1	11.1 %	1	16.7 %
Total	9	100.0 %	6	100.0 %

3.3. Evaluation criteria

3.3.1. Direct microscopic examination result among fingernails

Direct microscopic examination result among fingernails after the last session of laser therapy was positive in only one patient (11.1%), while the remaining 9 (88.9%) patients had negative results. There is a statistical significant difference between direct microscopic examination before and after laser therapy (*p* value < 0.05).

Table 3.4 Distributions of patients with onychomycosis according to direct microscopic examination result among fingernails.

Direct microscopic examination	Frequency	Percent%
Positive	1	11.1%
Negative	8	88.9%
Total	9	100.0%

P value = 0.000

3.3.2. Direct microscopic examination among toenails:

Direct microscopic examination result among toenails after the last session of laser therapy was positive in 2 patients (33.3%), while the remaining 4 patients (66.7%) had negative results. There is a statistical significant difference between direct microscopic examination before and after laser therapy (*p* value < 0.05).

Table 3.5 Distributions of patients with onychomycosis according to Direct Microscopic Examination result among toenails.

Direct microscopic examination	**Frequency**	**Percent**
Positive	2	33.3 %
Negative	4	66.7 %
Total	6	100.0 %

P value = 0.025

- When we compare this findings with the previous studies; the mycological improvement after LPNY laser appeared as 33-98.8% in different studies In vitro researches using Nd:YAG laser, Vural (Vural *et al.*, 2008) stated that the proliferation rate of Trichophyton rubrum decreased when treated by QSNY laser. However, in research conducted by Hees (Hees et al. 2012) using the same parameter, reported that LPNY laser, did not have any effect in decreasing the proliferation of T. rubrum. Kozarev and Vižintin (Kozarev and Vižintin, 2010) investigate 72 patients with 194 affected nails, treated with LPNY. Laser treatment consisted of four sessions with one week interval. The fluences applied were 35-40 J/cm^2 at laser PD 35ms and frequency 1Hz. On 3rd months follow up 95,8% patients were cleared of all fungal infections. Furthermore, Moon (Moon, *et al.* 2014) applied long-pulsed 1064-nm Nd:YAG laser on 43 nails with onychomycosis (13 patients) in treatment sessions performed at 4-week intervals. KOH test was done one month after the final treatment, 30 of the 43 fingernails and toenails had negative result. In adition Yang Xu (Xu *et al.*, 2014)compered between oral terbinfeine and Nd-YAG laser. He studed 53 patients, with a total of 90 infected nails. They were randomly divided into 3 treatment groups: the T group received oral terbinafine, the L group received long-pulsed Nd:YAG laser treatment, and the T + L group received both treatments. He evaluated the mycological clearance rate (MCR). The MCR increased in all 3 groups in a time-dependent manner. The MCR of the T + L group were significantly higher than those of the T group and the L group at weeks 8, 12, 16, and 24 ($p < .05$). In another study done by Wanitphakdeedecha (Wanitphakdeedecha et al., 2015) Sixty-four onychomycotic nails (35 patients) were evaluated. The first treatment cycle involved treatment with a long-pulsed 1064-nm Nd:YAG laser in four sessions at 1-week intervals. A KOH examination and fungal culture were performed every week during this treatment course and then at one month follow-up visit. The cure rate at the 1-month follow-up visit was 63.5%; this rate dropped to 57.7 and 51.9% at the 3- and 6-month follow-up visits, respectively. Also Kim (Kim *et al.*, 2016) studed fourty nails in 13 patients with severe onychomycosis were divided into two groups. Each group was received eight treatment sessions at one-week intervals with 1,064nm LPNY laser. Parameters for group A were 0.3ms pulse duration, 5mm spot size, 16 J/cm^2 fluence and 10Hz frequency, and those for group B were 0.6ms pulse duration, 2mm spot size, 225 J/cm^2 fluence and 5Hz frequency. Mycological clearance were evaluated

at 12 and 24 weeks after initial treatment. Mycological positive rates at 24 weeks were approximately 40% in both groups. From this study it is clear that, inspite of the high fluence used in group B, there was no obvious difference in the mycological clearance between the two groups. In a study conducted by Li (Li *et al*., 2016), the patients received treatment with oral itraconazole in conjunction with long-pulsed Nd:YAG 1064-nm laser treatment at the nails of the unilateral limb once a week for a total of four times. A total of 84 affected nails were divided into Group A (mild to moderate) and Group B (severe) according to disease severity. In Group A, the fungal culture results were significantly different between the combination treatment and control groups at the 8^{th} week ($P < 0.05$) , while in Group B, the fungal culture results were significantly different between the combination treatment and control groups at the 16^{th} ($P < 0.05$) but not at the 8^{th} or 24th weeks. Okan (Okan *et al*., 2017) studied thirty patients with mycologically confirmed onychomycosis had received long- pulsed 1064-nm Nd:YAG laser therapy. Spot diameter of 4 mm at a speed of 25 mm/sec once weekly for 4 weeks using fluencies ranging from 40 to 60 J/cm2. At the end of the study, mycologic cure was achieved in (60%) of the patients. In contarary to all previous studies, Hollmig *et al.*, 2014, mentioned clearly that there was no significant mycological culture clearance with 1064-nm Nd-YAG laser compared with control. It was a randomized, controlled, single-center trial comparing 2 treatments with 1064-nm Nd-YAG laser (fluence of 5 J/cm^2, rate of 6 Hz) spaced two weeks apart versus no treatment in 27 patients (N = 125 affected nails) with clinical and mycological diagnosis of onychomycosis. The different result in this study may be due to the few number of sessions (2 sessions) that are not enough to kill the fungii (the number of session in the previous studies range between 4-8). Also the low fluence used (5j/cm^2) may participate in this results, most studies had used a fluence between 40-60j/cm^2. All the studies mentioned above, except the last one, agreed in general with our results in that long pulse Nd-YAG can lead to mycological clearance in most of the patients . The difference in the cure rate may be due to the use of different laser parameters, numbers of sessions, period of follow up. Also, a possibility of false negative mycological test might lead to false results.

3.3.3. Clinical improvement among fingernails

Seven patients (77.8%) with fingernails involvement achieved clinical improvement while 2 patients (22.2%) not improved. There is a statistical significant difference in clinical improvement before and after laser therapy (*p* value < 0.05).

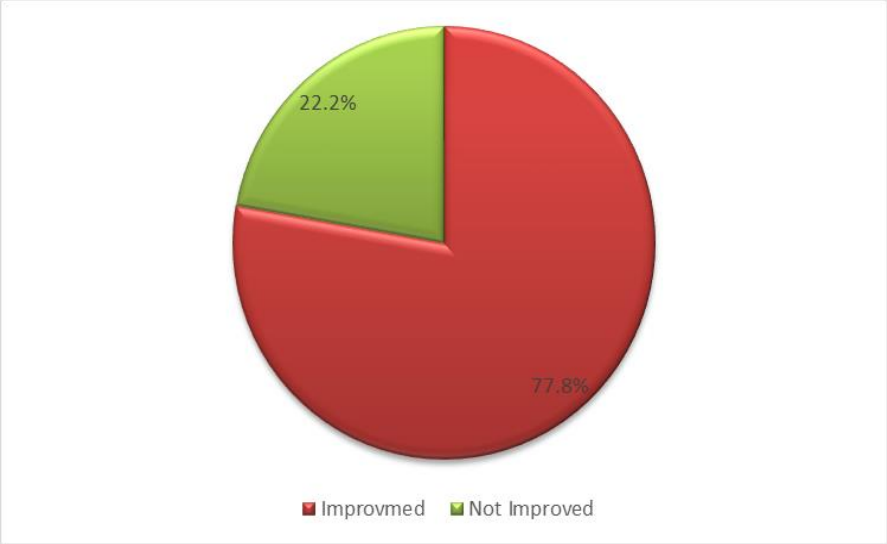


Figure 3.5 Distribution of patient with onychomycosis according to clinical improvement among fingernails.

P value = 0.001

3.3.4. Clinical improvement among toenails:

A 2 patients (33.3%) with toenails involvement achieved clinical improvement while 4 patients (66.7%) not improved. There is no statistical significant difference in clinical improvement before and after laser therapy (*p* value > 0.05).

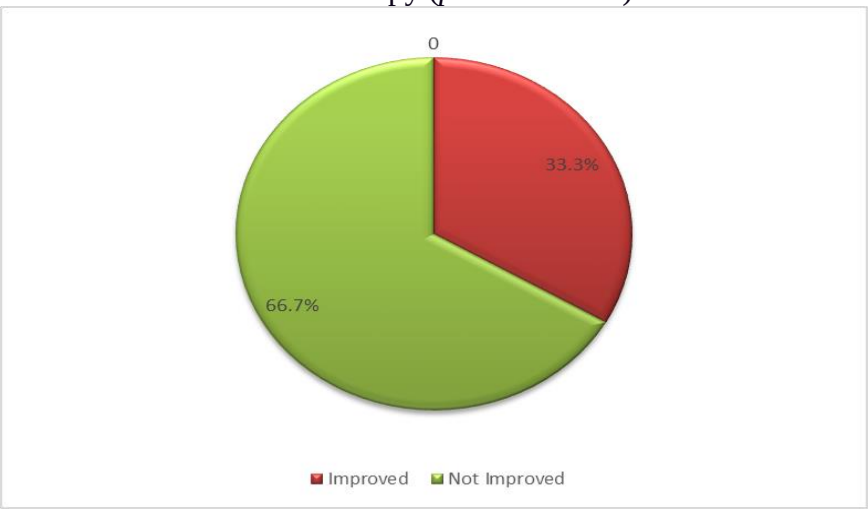


Figure 3.6 Distribution of patients with onychomycosis according to clinical improvement among toe nails

P value = 0.175

- When comparing this results with the previous studies; in vivo researches report that; the clinical improvement after LPNY laser treatment rang between (50-100)% . In this study 7 patients (77.8%) of the fingernails showed statistically significant difference in clinical improvements (p value <0.001) while 2 patients (33.3%) of the toenails showed clinical improvement, this is was not statistically significant (p value<0.175). This it might suggest that the variation of the thickness of the nail plate between fingernail and toe nail has played a major factor in the final result. Moon (Moon *et al.*, 2014) found in all patients, the extent of the fingernails and toenails affected by the disease gradually decreased as treatment continued. In adition Yang Xu (Xu *et al.*, 2014) found that the clinical clearance rate (CCR) increased in all 3 groups in a time-dependent manner. CCR of the T + L group were significantly higher than those of the T group and the L group at weeks 8, 12, 16, and 24 (p <.05). On the other hand, Gupta (Gupta and Paquet, 2015) found a temporary improvement in the appearance of the target nail in (78%) of patients and the affected area of the nail plate was reduced by at least 50% from baseline in (46%) of patients. Also Li study (Li *et al*., 2016), found no statistically significant difference in clinical efficacy between the combination treatment and control group in patients with mild to moderate onychomycosis (p > .05), however, the difference in clinical efficacy between the combination treatment and control groups in the patients with severe onychomycosis was significant (p < .05). On the otherhand, Kim (Kim *et al.*, 2016) found clinical improvement at 12 and 24 weeks was 47.6% and 57.1% in group A(ressived 8 sessions), 26.3% and 36.8% in group B(ressived 4 sessions). on the otherhand Piccolo (Piccolo et al., 2017) used different method in clinical evaluation. He enrolled twenty patients treated with a long-pulsed 1064-nm Nd:YAG laser, at intervals of one week, for a total of four sessions. Evaluation of patients was done by dermatoscopy. In fourteen patients (70%), excellent results were obtained with a significant reduction of chromonychia, onycholysis, opacity, longitudinal striae, and jagged proximal edge. All the mentioned studies are agreed upon Nd- YAG laser lead to clinical improvement of the appearance of the nails. The difference in the clinical improvemet rate may be due to the different clinical evaluation scales used by authors. Also the follow up period is very important to determine the clinical improvement. Because nails which are structurally abnormal can only clear by outgrowth of the dystrophic component and replacement by newly-created, normal-appearing nail. The mean growth rate for nails in healthy

U.S. adults is 1.5 mm per month for toe nails, and (3-3.5) mm per month for finger nails. Based on this mean growth rate, the ideal effective treatment would be expected to yield a fully replaced, clear fingernail in a healthy adult after approximately 6 months, and a fully replaced, clear great toe nail approximately 12 months after the initiation of treatment (Ogden, 2016). Therefore reassessment after 6 month for the fingernails and 12 month for thee toenails is very important to determine the real response to the treatment.

3.3.5. Patients satisfaction among fingernails

Regarding patients satisfaction among fingernails, 3 patients (33.3%) with fingernails involvement were satisfied with the treatment while 6 patients (66.7%) were not satisfied**.** There is no statistical significant difference inpatients satisfaction before and after laser therapy (*p* value > 0.05).

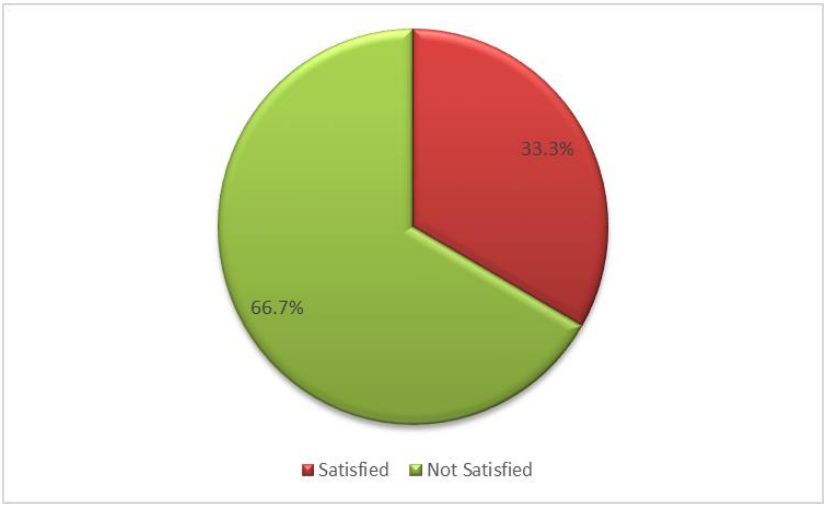


Figure 3.7 Distribution of patients with onychomycosis according to the satisfaction among fingernails.

P value = 0.081

3.3.6. Patients satisfaction among toenails:

Regarding patients satisfaction among toenails, one patients (16.7%) with toenails involvement were satisfied with the treatment while 5 patients (83.3%) were not satisfied**.** There is no statistical significant difference inpatients satisfaction before and after laser therapy (*p* value > 0.05).

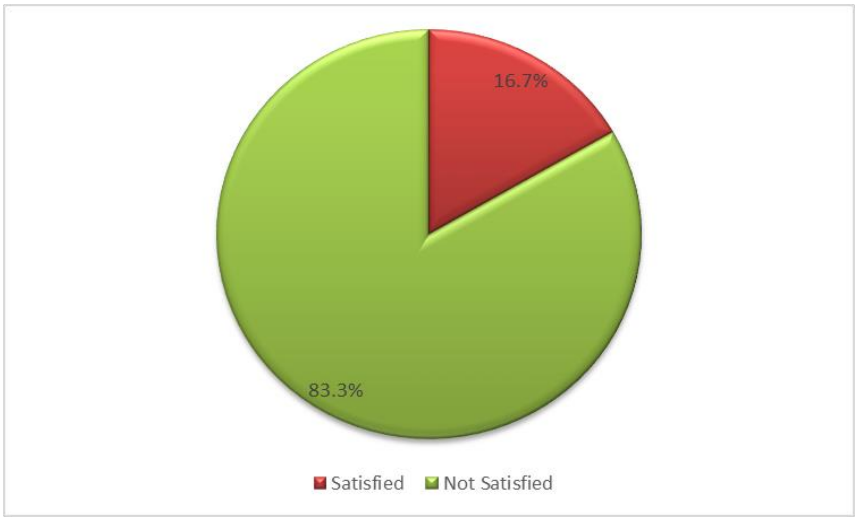


Figure 3.8 Distribution of patients with onychomycosis according to satisfaction among toenails.

P value = 0.363

- In this study the majority of patients were not satisfied with the treatment.). In contrast to this result Zhang (Zhang *et al.*, 2012) found six generally satisfied, sixteen satisfied, seven very satisfied and four patients were not satisfied,. Also Moon (Moon *et al.*, 2014) found high degree of satisfaction among his patients. Nine patients responded to the question about degree of satisfaction with satisfactory, and four with very satisfactory. The different results may be because patient's satisfaction is highly subjective, it depends on patient expectation. Also the assessment of the satisfaction before the complete replacement of the affected nails by new nail may affect the results.

3.3.7. Final response to the treatment among fingernails and toe nails

In patients with fingernails involvement excellent response was achieved in 2 patients (22.2%), good response was achieved in 5 patients (55.6%) and poor response was achieved in 2 patients (22.2%). While in patients with toenails involvement, excellent response was not achieved by any patient (0%), good response was achieved in 2 patients (33.3%), poor response was achieved in 2 patients (33.3%) and no response was achieved in 2 (33.4%) patients

Table 3.6 Distribution of patients with onychomycosis according to the final response among fingernails and toenails

Final response	**Fingernails**		**Toenails**	
	Frequency	Percent	Frequency	Present
Excellent	3	33.3%	1	16.7%
Good	4	44.5%	1	16.7%
Poor	2	22.2%	2	33.3%
No response	0	0%	2	33.3%
Total	9	100%	6	100%

The study found that all the patients had marked improvement of subungal hyperkeratosis after the last session.

Two patients who had total nail dystrophy, didn't show any clinical or mycological improvement.

Except of mild pain during the sessions, none of the ten patients had experienced any other side effects. This is agreed with Kozarev J and Vižintin (Kozarev J and Vižintin, 2010) whereas they found most of patients in average, reported mild pain, while none reported severe or intolerable pain. Also Wanitphakdeedecha (Wanitphakdeedecha et al., 2015) found treatment was well tolerated by the patients, and most of them reported only mild (34.4%) to moderate (40.6%) pain during the laser procedure.

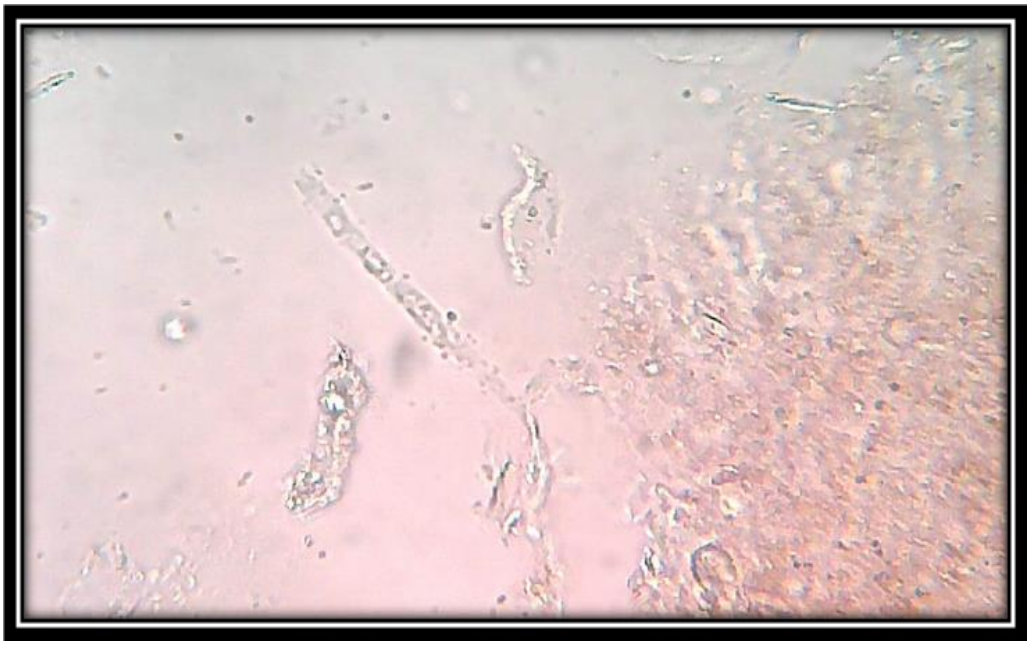


Figure 3.9 Septate hyphea on direct KOH examination.

1

2

3

Figure 3.10 Finger nail befor and after treatmen; picture 1 before , picture 2 after the 2nd session , picture 3 after the 4th session.

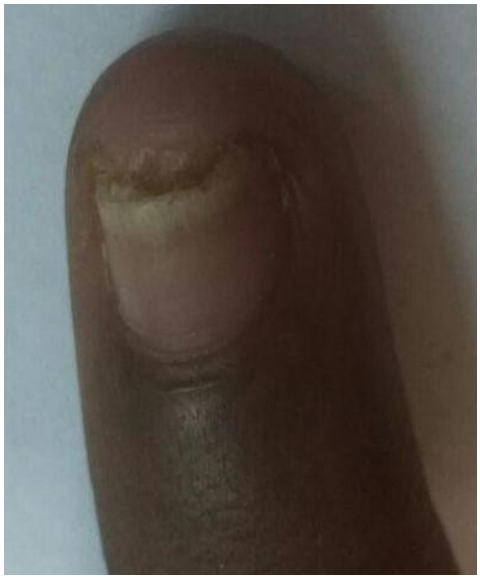
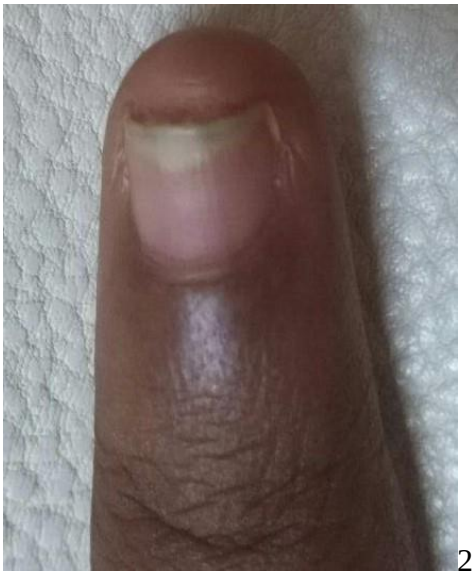
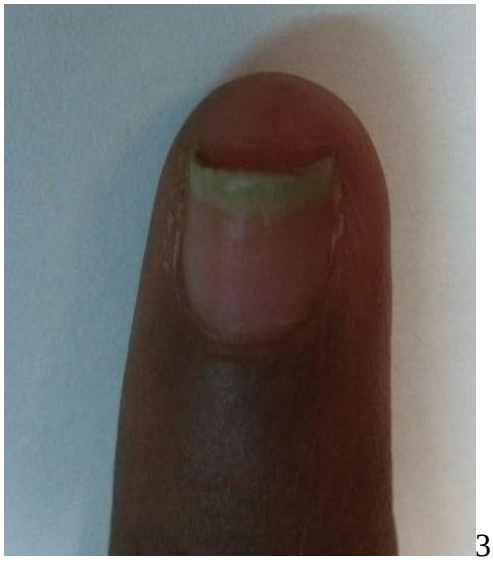
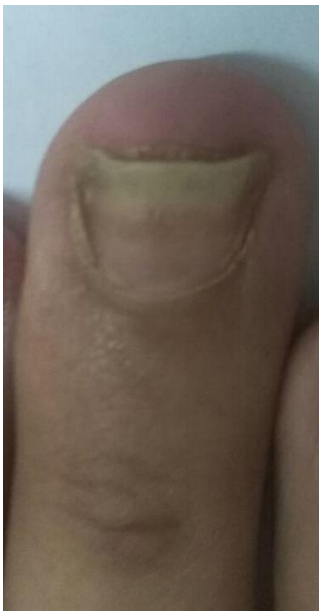

1

2

3

Figure 3.11 Finger nail befor and after treatmen; picture 1 before , picture 2 after the 2 session , picture 3 after the 4 session.

1



2

3

Figure 3.12 Finger nail befor and after treatmen; picture 1 before , picture 2nd after the 2 session , picture 3 after the 4th session.


1

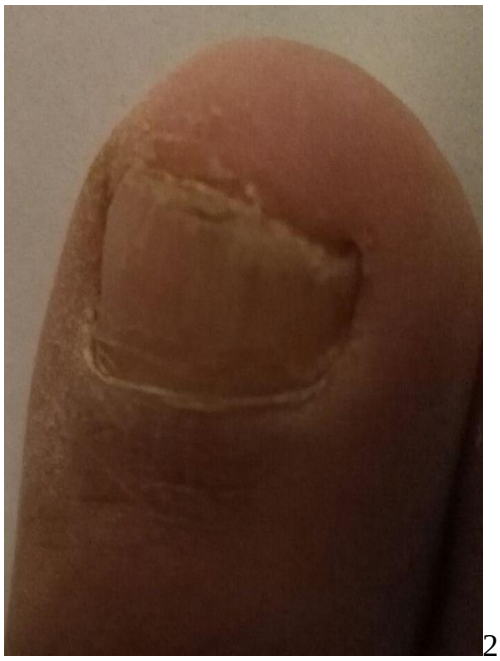

2

Figure 3.13 Toe nail befor and after treatmen; picture 1 before , picture 3 after the 4th session.

Conclusion

This study evaluated the effects of long-pulsed Nd-YAG laser 1064-nm in patients with onychomycosis. There was significant difference between the results of direct microscopic examination before and after treatment in both finger and toe nails. This may indicate the efficacy of Nd-YAG laser in the treatment of onychomycosis. However, the clinical improvement was significantly different among finger nails, while no significant result was obtained among toe nails. Most of the patients were not satisfied with the treatment results. There were no notable adverse effects, except of occasional mild pain during the sessions of treatment. Laser is a safe treatment that may be especially useful in patients with liver diseases. Further large case control studies are needed in order to confirm our results.

Recommendations

- Onychomycosis is an important health problem, it may be controlled by education of the patients about their nails changes, treatment options and avoidance of precipitating factors.
- Use of Nd - YAG laser as treatment option for onychomycosis may be safe and effective, especially for the patients with liver diseases, or in case of failure of antifungal drugs.
- Control Randomize Trials with large population, more laser sessions and longer follow up period are highly recommended.
- Up to one year follow up is recommended to determine the incidence of recurrence.
- Mycological tests, like culture or PCR are better to be done to confirm the results obtained from direct microscopic examinations and to avoid false negative results.

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Structured interview sheet:

Sudan University of science and technology
Laser Institute
Post graduate diploma of Laser Applications in Medicine

Treatment of Onychomycosis with Nd – Yag laser 1064 nm – Sudan 2018

Structured interview sheet

Serial NO: ☐ ☐ ☐

- **Personal data**
- Age in years: ☐ ☐
- Gender: Male ☐ Female ☐
- Marital status: Single ☐ Married ☐ Divorced ☐
- Occupation:……

Nail complains:

Thickening ☐ Change in color ☐ Brittle ☐ Disfigurement ☐

Pain ☐ No symptoms ☐

Duration of nail changes: Weeks ☐ Months ☐ years ☐

Family history of the same condition: Yes ☐ NO ☐

Socioeconomic status: High ☐ Moderate ☐ Low ☐

Drug history of antifungals:

Topical ☐ systemic ☐ not present ☐

Duration of therapy: three month ☐ six month ☐ more ☐

2.Clinical examination:

Nail examination:

No of affected nails:

Finger nails: RT hand ( ) LF hand ( )

Toe nails: RT foot ( ) LF foot ( )

Onychomycosis nail changes:

Finger nails: Discoloration☐ Thickened nail plate ☐ Powdery white patches☐

Leukonychia☐ Total nail dystrophy ☐ Paronychia☐

Toe nails: Discoloration ☐ Thickened nail plate ☐ Powdery white patches☐

Leukonychia☐ Total nail dystrophy ☐ Paronychia ☐

Area of Nail involvement:

Proximal ☐ distal ☐ all nail plate ☐

Type of onychomycosis:

Distal and lateral subungual onychomycosis ☐

Superficial white onychomycosis ☐

Proximal subungual onychomycosis ☐

Endonyx onychomycosis ☐

Total dystrophic onychomycosis ☐

Number of laser session:……

Evaluation criteria:……..

1. Direct microscopic examination

   Positive ☐ negative ☐

2. Clinical improvement

   Improved ☐ not improved ☐

3. Patient satisfaction:

   Satisfied ☐ not satisfied ☐

Consent:

استمارة الموافقة المشاركه في البحث

عنوان البحث:علاج فطريات الاظافر بواسطة الليزر

اسم الباحث: د. سلافه محمد عثمان حمد

رقم الهاتف: 0924067500

مشرف علي البحث: د. شذي يوسف – د. سهاد سعد الوكيل

مكان البحث:مستشفي الخرطوم للامراض الجلديه والتناسليه

- فطريات الأظافر من الأمراض المنشرة ولها كثير من الاثار علي المرضي . العلاج بالليزر اثبت فعاليتة في العديد من الدراسات مع قلة الأثار الجانبية بالمقارنة مع الأدوية الفموية .
- تهدف هذه الدراسة لتقصي اثر العلاج بالليزر علي فطريات الأظافر.
- سوف نقوم في هذه الدراسة بأخذ عينه من الظفر وإرسالها الي المعمل حيث يتم فحصها مباشرة تحت المجهر كما ويتم تزريعها في الاوساط الزرعيه المناسبه للفطريات حتي نحصل علي نتائج دقيقه بإذن الله.
- اذا وافقت علي المشاركه في هذا البحث سوف يتم اخذ عينه من الأظافربواسطة اله خاصه وذلك بعد اجراء التعقيم اللازم ويتم الاحتفاظ بها لحين اجراء الفحص المطلوب.
- قد نحتاج لبعض الصور بغرض عرضها في البحث, ونلتزم باخفاء الملامح الشخصيه للمشارك ان كانت ظاهره.
- المعلومة المدونة في الاستبيان سوف تبقي سريه ويتم تداول المعلومات فقط عن طريق الرقم المتسلسل وليس الاسم .
- مشاركتك في البحث قد تساهم في تطوير الخدمات الطبيه , لكن بالتاكيد عدم المشاركه لن يؤثر علي الخدمات المقدمه اليك.
- هذه الاستماره مكونه من نسختين الاولي لدي الباحث والثانيه لدي المشارك اذا احتجتم لاي استفسار الرجاء الاتصال برقم الهاتف الموجود اعلي الورقه .

اسم المشارك في البحث وتوقيعة :.....

Equipments:

Autoclave Grggina ad George LTD- England

Incubator Torrepic NAPJ (CR) HAIY

Microscope Olympus CH 20 - Japan

Bunsen flam

Pipettes. China

5ml sterile syringes Sudan

Slides bomix China

Cover slips China

Disposable Petri dishes China

Flasks. India

Gloves

70% alcohol pads

Cotton

Filter papers

Glass bottles

Mycological needle

Forceps

Methyline blue

KOH 20%